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ORIGINAL ARTICLE

Could ICG-aided robotic cholecystectomy reduce the rate of open conversion reported with laparoscopic approach? A head to head comparison of the largest single institution studies

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Abstract Comparative studies between robotic and laparoscopic cholecystectomy (LC) focus heavily on economic considerations under the assumption of comparable clinical outcomes. Advancement of the robotic technique and the further widespread use of this approach suggest a need for newer comparison studies. 676 ICG-aided robotic cholecystectomies (ICG-aided RC) performed at the University of Illinois at Chicago (UIC) Division of General, Minimally Invasive and Robotic Surgery were compiled retrospectively. Additionally, 289 LC were similarly obtained. Data were compared to the largest single institution LC data sets from within the US and abroad. Statistically significant variations were found between UIC-RC and UIC-LC in minor biliary injuries ($p = 0.049$), overall open conversion ($p \leq 0.001$), open conversion in the acute setting ($p = 0.002$), and mean blood loss ($p < 0.001$). UIC-RC open conversions were also significantly lower than Greenville Health System LC ($p \leq 0.001$). Additionally, UIC ICG-RC resulted in the lowest percentages of major biliary injuries (0 %) and highest percentage of biliary anomalies identified (2.07 %). ICG-aided cholangiography and the technical advantages associated with the robotic platform may significantly decrease the rate of open conversion in both the acute and non-acute setting. The sample size discrepancy and the non-randomized nature of our study do not allow for drawing definitive conclusions.

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Introduction

Numerous studies have compared the robotic vs. laparoscopic cholecystectomy (LC) approaches. These comparative studies focus heavily on economic considerations due to the higher cost associated with the acquisition of the robotic platform, under the assumption of no difference in clinical outcomes when compared to the laparoscopic approach [1–3]. The introduction of routine cholangiography through the use of ICG fluorescence represents a significant advancement in the robotic technique that some argue could translate in improved clinical outcomes [4, 5]. Furthermore, the number of cholecystectomies performed with the ICG-aided robotic approach has been significantly increasing over the past few years [6], and a more accurate comparison can now be implemented between the otherwise greater and mismatching numbers of the laparoscopic vs. robotic approach. Therefore, newer comparison studies are important to reflect these developments.

We decided to investigate the matter by comparing the outcomes of robotic cholecystectomy with routine use of ICG (ICG-aided RC) vs. LC within our center, as well as between the largest single institution LC data sets from within the US and abroad.

Methods

A total of 965 cholecystectomy cases from University of Illinois at Chicago (UIC) Division of General, Minimally Invasive and Robotic Surgery were retrospectively compiled. Inclusion criteria for the study were all patients undergoing cholecystectomy as either a primary or secondary operation during the study date ranges outlined below. Exclusion criteria were robotic cases occurring within the data collection range where ICG was not administered based on timing constraints. In total, 676 ICG-aided RC operations performed between July 1, 2011 and June 10, 2015 were collected, representing the largest data set of its kind to our knowledge. Additionally, 289 LC cases performed at UIC between September 10, 2008 and June 22, 2015 were similarly obtained. UIC is a high volume robotic center performing over 500 robotic cases a year, but also performs LC based on the preference of the patient or surgeon, availability of the robotic platform and staff at affiliated medical centers, and as part of residency training exposure. All cases included in the study were performed by the same surgical team at UIC consisting of members with experience performing at least 125 cases in both the laparoscopic and robotic approaches and aided by surgical residents in training, who have completed formal training of basic skills in both laparoscopic and robotic techniques. Demographics gathered included gender, age, BMI, and ASA class and are detailed in Table 1. Outcome data collected included blood loss, biliary anomalies encountered, diagnosis, length of hospital stay, open conversions and any complications. Major biliary injuries were those classified as Strasberg types D and E, while minor biliary injuries included Strasberg types A, B, and C. Mean blood loss and length of hospital stay were calculated in cases where cholecystectomy was the primary operation and no major biliary complications occurred. Data was compiled in Microsoft Excel spreadsheets and then compared to the data published by Le, Smith, and Johnson (Greenville Hospital System University Medical Center, GHS), as well as Tantia et al. (ILS Hospitals, Kolkata, India) [7, 8]. A literature review conducted through PubMed found the Le study to represent the largest US-based single center LC experience to our knowledge with 3371 cases and Tantia et al. represent the world's largest single center LC experience with 13,305 cases.

Statistical analysis

All data analysis was conducted using SAS software 9.4 (SAS institute Inc., Cary, NC, USA).

The descriptive statistics are provided for the outcomes of interests. For binary variables, Chi square test was performed to test the between-group (robotic vs. laparoscopic) difference. An examination of histograms revealed that days of hospitalization and blood loss do not follow normal distribution, and skewed to large values. The generalized linear model with Gamma distribution was applied to test the between-group difference for hospital stay and blood loss. For the demographic data, a two-sample t test is used for continuous variable, and Chi square test is used for categorical variable.

Surgical technique and fluorescent imaging system

The Da Vinci® Fluorescence Imaging Vision system allows the surgeon to obtain real-time, 3D high definition images of the surgical field. The platform includes a surgical endoscope that provides Firefly® fluorescence and white light imaging, an endoscopic illuminator, and a stereoscopic camera head. The same imaging capabilities were available in both the single site and multi-port techniques, which were conducted using the standard techniques for each. Patients were administered 2.5 mg of the ICG contrast 45 min prior to the operation to allow time for the dye to be taken up by the structures of interest. During

Table 1 Characteristics of laparoscopic and robotic surgery cases

Variables	Laparoscopic mean (SD) or *N* (%)	Robotic mean (SD) or *N* (%)	*p* value
N = 965	289	676	
Age	40.75 (15.44)	43.91 (16.12)	0.005
Female	225 (77.85)	496 (73.37)	0.142
BMI	31.19 (7.76)	32.28 (8.57)	0.065
ASA Class			
1	70 (24.42)	122 (18.24)	0.019
2	164 (56.75)	378 (56.50)	
3	48 (16.61)	160 (23.92)	
4	7 (2.42)	9 (1.35)	
1	70 (24.42)	122 (18.24)	0.034 (pair)
2	164 (56.75)	378 (56.50)	0.944 (pair)
3	48 (16.61)	160 (23.92)	0.012 (pair)
4	7 (2.42)	9 (1.35)	0.234 (pair)

the operation, surgeons were then able to visualize the anatomy in either fluorescent or normal lighting modes by switching between them at the console. The critical views of Calot's triangle included in this study were obtained in fluorescent mode in each operation performed at UIC.

Results

Statistically significant variations were found between UIC-RC and UIC-LC in four categories including minor biliary injuries ($p = 0.049$), overall open conversion ($p \leq 0.001$), open conversion in the acute setting ($p = 0.002$), and mean blood loss ($p < 0.001$). Overall, UIC-RC open conversions were also significantly lower than Greenville Hospital System LC ($p \leq 0.001$). Additionally, UIC ICG-aided RC resulted in the lowest percentages of major biliary injuries (0 %) and identified the highest percentage of biliary anomalies during the operation (2.07 %). LC data from UIC comprised the highest percentage of both major biliary injuries and open conversions (0.34 and 4.5 %, respectively). Data from the four studies is presented in Table 2.

Discussion

Biliary injury is the primary area of concern with any cholecystectomy. Proper identification of the biliary anatomy is the key requirement to avoid such injuries and depending on which surgical technique is used, various forms of imaging are available to aid in obtaining the critical views.

Traditional intraoperative cholangiogram (IOC) represents the gold standard diagnostic modality for the identification of the biliary anatomy in LC, but it is not without its drawbacks. Currently, IOC is only used in certain situations, mainly unclear biliary anatomy, and its routine use has been phased out due to a lack of supporting evidence [9–12]. Furthermore, IOC is associated with additional costs (on average >$700) and a number of accompanying risks [9]. There is a learning curve associated with training surgeons to perform and properly interpret IOC, with studies showing that only 57 % of IOC images are correctly interpreted [13]. Risks associated with exposure to radiation for the patient and staff and a potential for allergic reaction to the contrast dye are also considerations. Technically, an IOC cannot be performed and interpreted in real time due to the cumbersome and time-consuming setup necessary to perform the test (C-arm, biliary catheter placement, lead protective gear, etc.).

The ICG-aided cholangiography presents no radiation risks, can be performed and interpreted in real time and has an associated risk for allergic reaction of 0.003 % in doses that exceed 0.5 mg/kg [14]. The ICG-aided cholangiography may also detect biliary anomalies that would have otherwise been missed without the routine implementation of traditional IOC. In our study, 2.07 % of ICG-aided RC patients were found to possess a biliary anomaly, compared to 0.69 % of LC with IOC patients at UIC (information not available from Greenville Hospital System or ILS studies). The detection of these anomalies may have played a role in

Table 2 Results and *P* values

	UIC RC	UIC LC	*p* value (UIC-RC/ UIC-LC)	GHS LC	*p* value (UIC-RC/ GHS LC)	ILS LC	*p* value (UIC-RC/ ILS LC)
Number of total cases: number of acute cholecystitis or gangrenous cholecystitis cases	676:131	289:94	–	3371: –	–	13,305: –	–
# Of major biliary injuries*/percentage	0/0.0 %	1/0.34 %	0.126	4/0.12 %	0.368	20/0.15 %	0.3125
# Of minor biliary injuries**/percentage	1/0.15 %	3/1.04 %	**0.049**	–	–	32/0.24 %	0.631
# Open conversion/percentage	1/0.15 %	13/4.5 %	**<0.001**	86/2.6 %	**<0.001**	–	–
# Open conversions in acute cholecystitis and gangrenous cholecystitis setting/percentage	1/0.76 %	9/9.57 %	**0.002**	–	–	–	–
# Of biliary anomalies identified intraoperative/ percentage	14/2.07 %	2/0.69 %^	0.170	–	–	–	–
Mean hospital stay (no complications) days (standard deviation)	1.21 (1.60)	1.20 (1.48)	0.892	–	–	2	–
Mean blood loss mL (standard deviation)	14.37 (27.26)	21.08 (72.22)	**<.001**	–	–	–	–

Bold indicates a statistically significant finding

* Injuries classified as Strasberg Types D or E

** Injuries classified as Strasberg Types A, B or C

^ Identified via intraoperative cholangiography the avoidance of any major biliary injury during ICG-aided RC. Despite the benefits, some limitations to ICG-aided cholangiography have been reported in the literature, specifically reduced tissue penetration of the near infrared light, which might require further tissue dissection in obese patients or in the acute cholecystitis setting [14]. Unfortunately, pre-dissection was not uniformly documented in our operative reports in a manner that would allow for this analysis.

The use of ICG technology is also possible with the laparoscopic approach; however, the technique is not routinely used today and studies only have limited patient sample sizes to report [15]. At this stage of development, the literature on intraoperative ICG in LC focuses primarily on the efficacy of technology and its ability to identify structures and less on clinical outcomes. Therefore, a direct comparison of ICG-aided RC and LC for this paper was not possible. Additionally, when dealing with small patient sample sizes an absence of injury prevalence is skewed when compared to studies with larger data sets [16]. From a cost/benefit comparison standpoint, the best option provided for intraoperative ICG-aided cholangiography in LC is arguably the PINPOINT® tower from Novadaq, which requires the purchase of a $100,000 imaging tower, $3500 endoscope, and the purchase of disposable kits for each procedure, all adding to the cost of the operation [17]. Novadaq is the same company that developed the FireFly® system for use with the da Vinci robotic platform, yet the PINPOINT® technology is still centered upon a 2D image in comparison to the 3D image provided through the robotic console (Fig. 1). While ICG-aided cholangiography is feasible in the laparoscopic approach, at this time traditional IOC remains the gold standard for the identification of biliary anatomy when necessary.

Despite all the mentioned benefits of the ICG-aided cholangiography, it is hard to believe that this diagnostic modality is the only reason, per se, for the significantly lower number of open conversions reported in the robotic setting when compared to our own LC experience and to the largest USA-based and abroad LC experiences. We believe that the technical advantages associated with the robotic platform, such as a greater vision of the field featuring 3D images that are filtered and cleaned up by a computer prior to being presented to the operator at the console, the availability of the Endowrist® that reproduces all the degrees of freedom of the human wrist and the routine use of the 3rd robotic arm that greatly facilitates exposure of the tissues, have all contributed to the significantly lower rate of open conversions in both the acute and non-acute setting. From the data collected, ICG-aided RC was converted in only 0.15 % of the overall cases, compared to 4.5 % of UIC-LC, and 2.6 % from Greenville Hospital System, both representing statistically

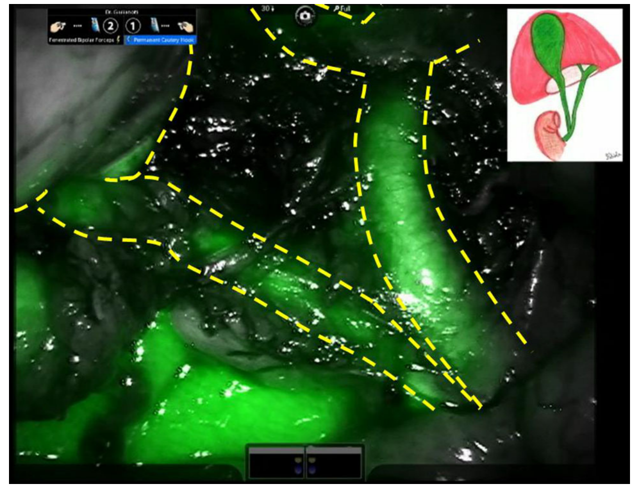

Fig. 1 Low and parallel course and union of the cystic duct with the common hepatic duct as seen during ICG-aided robotic cholecystectomy

significant differences. A deeper analysis of the data to include only the acute cases (including both acute cholecystitis and gangrenous cholecystitis) reveals a similar result with just one conversion out of 131 robotic cases, or 0.76 %, when compared to nine conversions out of 94 acute cases, or 9.57 %, from the UIC-LC data set, again yielding a statistically significant difference. Greenville Hospital System data did not specify preoperative diagnoses in their report and, therefore, could not be compared in this regard. The Tantia et al. study reported a 15 % conversion rate within the 52 biliary injuries encountered, but does not provide total open conversion figures and, therefore, cannot be directly compared with the other data sets for these results. This study is the first to compare open conversion in cholecystectomies; however, the results are in line with those published on conversion rates in colorectal surgery, where the robotic cases were converted at lower rates when compared to laparoscopic [18].

Demographic information from the UIC-RC and UIC-LC patients was also collected and analyzed to elucidate potential underlying patient selection bias from within the samples. Statistically significant differences between the groups included age and ASA class. Robotic patients were on average three years older and classified in a higher ASA bracket based largely on a significantly higher percentage of class III patients. There were no statistical differences appreciated between the groups for gender or BMI. This information reveals a strong similarity between the sampled groups that helps to eliminate potential confounding variables that may have played into the study findings. Although these basic demographics provide some clarity on the overall picture of the two sample groups studied, a lack of further analysis regarding co-morbidities and pre-operation diagnoses for the patients is a drawback of the study and limits the conclusions that can be drawn from the overall health of the patients' pre-operation.

A randomized, controlled and prospective trial is necessary to gather the definitive evidence in favor of one or the other approach. In general, it is difficult and challenging to perform a randomized and prospective trial in the surgical setting, and even more so in this case as the majority of patients coming to our surgical center are specifically requesting cholecystectomy with robotic approach. This is clearly a limitation of our retrospective study, which can still provide some useful insight about the hypothesis being investigated, especially in consideration of the fact that statistically significant differences were obtained in four different categories. We hope that sharing these findings with the rest of the surgical community could trigger further interest about this topic and perhaps encourage a prospective and randomized multicenter trial.

Another possible criticism worth discussing is represented by the potential bias related to the improving experience of the surgeons performing the ICG-aided RC over time. While this critique is a valuable component to consider, the fact that we have been performing, and still perform, both laparoscopic and robotic cholecystectomies and the timetable for both approaches included in the study is overlapping, as clearly described in our methods section, works to eliminate this potential bias. Additionally, it has been the same surgical team performing both procedures; therefore, any experience gap would be reflected in both approaches as there is no separate dedicated robotic vs. laparoscopic teams at our institution. The general surgery team at UIC also performs strictly laparoscopic cholecystectomies at affiliated institutions where there is no robotic console; however, this data is not included in this study.

Finally, some argue that robotic cholecystectomy may not be financially convenient, mainly due to the initial upfront costs associated with the acquisition of the robotic platform. However, RC has the potential to be just as cost effective as LC. The literature shows that high volume robotic centers that maximize their capacity have the potential to bring the costs of operating robotically down to that of laparoscopy [19]. As more operations are performed, the overhead associated with the high upfront cost of purchasing the robotic platform is further distributed and the single procedure costs to the hospital decrease accordingly. Although specific figures for cholecystectomy data are not readily available from high volume centers, other procedures have shown no significant overall cost differential between the robotic and laparoscopic approaches [2]. A more in-depth analysis into the true cost differential between robotic and LC in high volume centers was considered and is a worthwhile and valuable endeavor, but is beyond the aims of this particular paper.

Conclusions

Our study suggests that routine implementation of ICG-aided cholangiography, and the technical advantages associated with the robotic platform, may significantly decrease the rate of open conversion in both the acute and non-acute setting when compared to LC. Unfortunately, the sample size discrepancy and the non-randomized nature of our study do not allow for drawing definitive conclusions at this moment.

The reason for our sample size discrepancy resides on UIC being a high volume robotic center that performs significantly more ICG-aided RC than LC, in combination with a lack of electronic medical record data referring to LC performed prior to September 2008. Additionally, despite the Greenville Hospital System and ILS reports representing the largest laparoscopic experiences of their kind, the partial lack of data in these two studies represents an additional limitation of our study as it does not allow for a direct and full comparison of outcomes with our center's experience.

If our findings are confirmed by larger, prospective and randomized trials, a fair question that should be considered moving forward is whether or not it is ethical to use a technique that may be associated with a higher risk of complications solely due to its perceived financial benefits. Until then, definitive conclusions cannot be drawn on this specific matter.

Compliance with ethical standards

Conflict of interest Author Antonio Gangemi, Author Rick Danilkowicz, Author Fernando Enrique Elli, Author Francesco Maria Bianco, Author Mario Masrur and Author Pier Cristoforo Giulianotti declare that they have no conflict of interest pertinent to this study.

Research involving human participants and/or animals All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all patients for being included in the study.

Informed consent Informed consent was obtained from all individual participants included in the study.

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