

The laparoscopic Glissonian approach is safe and efficient when compared with standard laparoscopic liver resection: Results of an observational study over 7 years

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Objective. This study compares the Glissonian approach with the standard approach to laparoscopic liver resection for safety and efficacy.

Background. The standard laparoscopic approach to anatomic liver resection is the dissection of the elements of the Glissonian pedicle below the hilar plate. In contrast, the Glissonian approach identifies the intrahepatic pedicles by tentative clamping. Concerns have been raised about the safety of the Glissonian approach in laparoscopic liver surgery. The study was performed to examine the initial 7 years of experience in a single center with regard to safety and efficacy.

Methods. All consecutive patients undergoing laparoscopic liver resections from April 2007 to April 2014 at a single referral center for liver tumors were included. An observational comparison was performed between Glissonian and standard laparoscopic liver resections performed by the same team but during different eras. The primary endpoint was safety of the procedures as assessed by the recently published comprehensive complication index. Secondary endpoints were parameters of surgical efficacy, such as operating time, blood loss, blood transfusion, conversion rate, duration of hospitalization, and pathologic margin of the specimen.

Results. Between 2007 and 2014, 234 resections were performed laparoscopically at our institution, 120 using the conventional approach and 114 using the Glissonian approach. There was no difference in age, sex, tumor types, or comorbidities between the groups. The number of major liver resections was greater in the Glissonian group, yet there were fewer complications in the Glissonian group compared with the standard group ($P < .05$). Operative time was greater and more transfusions were given in the standard group; in addition, more patients had positive margins ($P < .01$). Overall hospital stay was less in the Glissonian group.

Conclusions. In the 7-year experience of a single center, the Glissonian approach is not less safe and may seem to offer advantages when compared with the standard laparoscopic approach. (Surgery 2016;■:■-■.)

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RECENT ADVANCES IN LAPAROSCOPIC DEVICES and greater experience have resulted in an increase in laparoscopic liver resection for all indications.¹⁻⁵ In most

Accepted for publication January 12, 2016.

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0039-6060/\$ - see front matter

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<http://dx.doi.org/10.1016/j.surg.2016.01.017>

centers, laparoscopic liver resections consist primarily of nonanatomic resections, right or left hemihepatectomies, and left lateral segmentectomies.¹⁻⁷ Anatomic second- or third-order resections are performed less commonly owing to the technical difficulties of controlling the segmental pedicles laparoscopically.⁸

The Glissonian approach to open liver resection was pioneered by Galperin and Karagiulian,⁹ Takasaki et al,¹⁰ and Launois and Jamieson,¹¹ and we

published a simplification of this technique to facilitate the selective clamping of Glissonian pedicles in the suprahilar area in 2003.^{12,13} Based on small incisions at anatomic landmarks, the new approach allowed the highly selective control of Glissonian pedicles without hilar or parenchymal dissection, and without the need for ultrasonographic or cholangiographic guidance.^{12,13} This landmark-guided anatomic approach allowed segmentectomies along lines of vascular demarcation in open liver surgery. Consequently, since 2007, we have also used the Glissonian approach for laparoscopic liver resections.^{14,15} Concerns have been voiced about the landmark-based approach owing to the possibility of bile duct injury, bile leak, or biliary stricture.

The aim with this study was to evaluate comprehensively 7 years of experience with this simplified approach in laparoscopic liver surgery from the standpoints of safety and surgical efficacy using a prospective database. The study also aimed to provide a systematic description of the laparoscopic Glissonian approach for different anatomic laparoscopic resections to provide a rational basis for future study.

METHODS

Study design and setting. This observational study compares 2 cohorts of patients at an urban referral center for liver tumors in São Paulo, Brazil. Patients with liver tumors undergoing liver resection were referred from a drawing area of approximately 8 million patients by 6 primary care, 3 oncologic, and 3 internal referrers. All patients undergoing liver resection at our institution are recorded in a database that is maintained prospectively by our HPB fellows and clinical study nurses; all patients are discussed in our multidisciplinary tumor board. Laparoscopic liver resections are proposed by the surgical team consisting of 3 surgeons and 2 fellows based on location and extent of disease. In this study, consecutive patients undergoing laparoscopic liver surgery by this team over the 7-year period between April 2007 and April 2014 were studied retrospectively (Fig 1). All patients had follow-up with data collection sheets in our surgical clinic, 2 oncology clinics, and primary care physician offices up to study closure in December 2014.

Operative technique. Exploration of the abdominal cavity and an ultrasonographic liver examination were performed in all cases. Patients are placed in the “French position” with legs spread and bent at the knees with the surgeon standing between the patient’s legs. Four trocars are

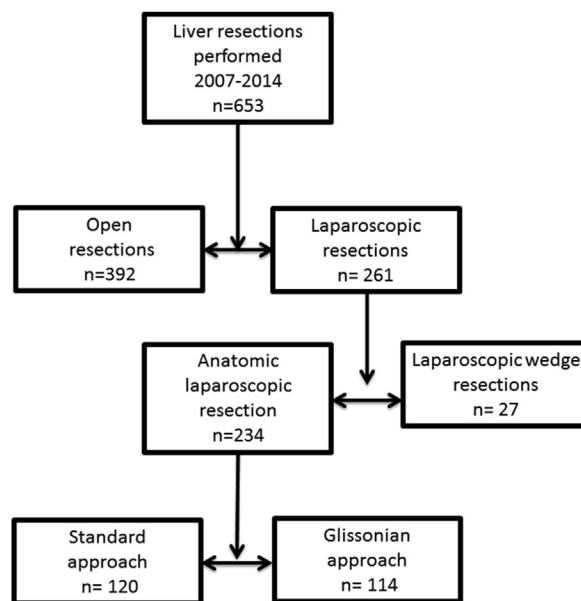


Fig 1. The flow diagram shows all referred patients undergoing surgery for liver tumors in our institution between 2007 and 2014, stratified by an open and laparoscopic approach.

inserted as described previously.^{14,15} If the gallbladder is in place, a cholecystectomy is performed, but the gallbladder may be kept for traction and exposure until the end of the procedure. The standard approach is performed by dissecting and transecting the respective hepatic artery and portal vein in right and left hemihepatectomies.^{16,17} For all other segmental resections, anatomic approximation was used with laparoscopic ultrasonography for determination of resection lines and parenchymal transection performed without hilar control. Parenchymal transection is performed using the harmonic scalpel (Ethicon, Cincinnati, OH), a bipolar clamp, and scissors with occasional ligaclips (Ethicon), and endostaplers (Ethicon) for large veins or Glissonian structures. In the Glissonian approach, we used 3 small liver incisions around the hilar plate according to specific anatomic landmarks.^{12,14} A small (3-mm) incision is performed directly cranial to the hilum, and a second incision (b in Fig 2, A) is performed on the right edge of the gallbladder bed. A third incision is made perpendicular to the hepatic hilum in the transition zone between segments 7 and 1 (c in Fig 2, A). By a combination of these 3 incisions (Fig 2, B), it is possible to control intrahepatically the Glissonian pedicle of the entire right hemiliver (a to c) or, selectively, the anterior (a to b) or posterior (b to c) sections of the right hemiliver. The approach for a right hepatectomy

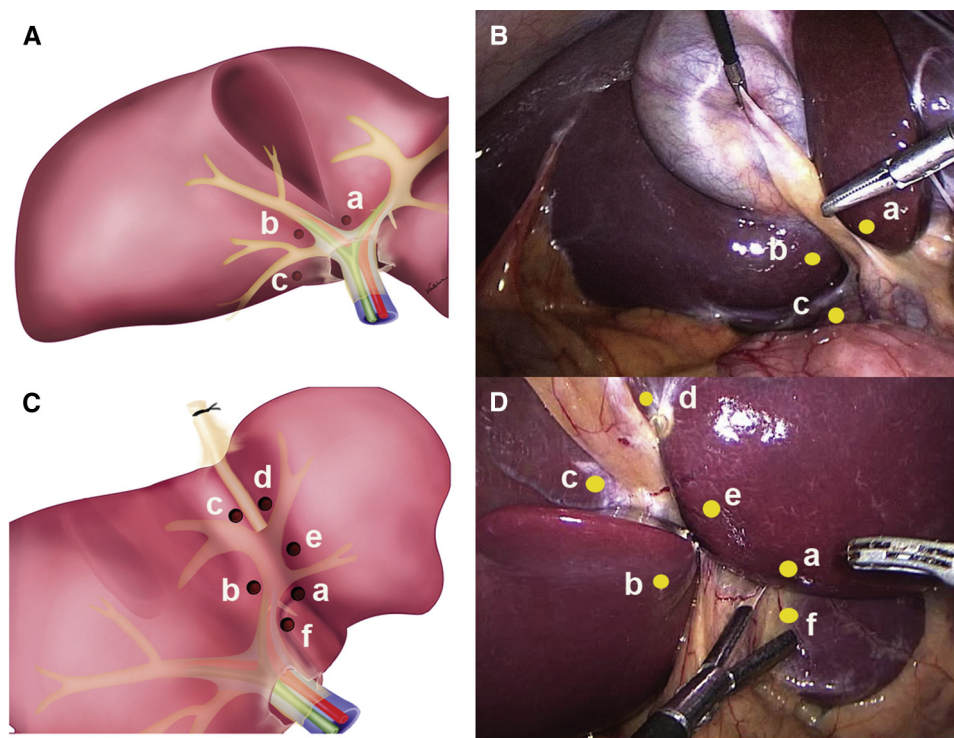


Fig 2. Diagrams and intraoperative view of the anatomic landmarks for laparoscopic right and left liver resections. *A*, Incisions for the intrahepatic approach to the right Glissonian pedicles. Three small incisions are used: (a) incision directly cranial to the hilum, (b) incision on the right edge of the gallbladder bed, and (c) incision on segment 7 perpendicular to the hepatic hilum. *B*, Intraoperative view showing the anatomic landmarks for access to the right Glissonian pedicles (*yellow spheres*). *C*, Incisions for the intrahepatic approach to the left Glissonian pedicles: (a) the caudal stump of the Arantius ligament, (b) the incision cranial to the hilum, (c) the base of the round ligament, right side, (d) the base of the round ligament, left side, (e) midway between sites *D* and *A*, and (f) caudate notch. *D*, Intraoperative view showing the anatomic landmarks for access to the left Glissonian pedicles (*yellow spheres*). (a) to (f), same as *C*.

is shown in [Figs 3, A and 4, A](#), right posterior sectionectomy (resection of segments 6 and 7) in [Figs 3, B and 4, B](#), and right anterior sectionectomy (resection of segments 5 and 8) in [Figs 3, C and 4, C](#).

To reach the Glissonian pedicles of the left liver, 6 small liver incisions can be used.^{13,15} The Arantius ligament is divided, and the caudal stump of the ligament is used as a landmark for the left Glissonian pedicle (a in [Fig 2, C and D](#)). A small (3-mm) anterior incision is made cranial to the hilum to the left (b in [Fig 2, C and D](#)), and the round ligament is retracted anteriorly, exposing the umbilical fissure between segments 3 and 4. Using the round ligament as a guide, 2 small incisions (c and d in [Fig 2, C and D](#)) are performed on the right and left margins of the round ligament. Another small incision can be performed midway between incisions a and d (e in [Fig 2, C and D](#)), which allows the individual resection of segments 2 and 3. Another incision over the edge of segment 1 (f in [Fig 2, C and D](#)) can be performed

to allow individual access to the pedicle to segment 1.

The laparoscopic Glissonian approach to segmentectomy 1 is shown in [Figs 3, D, and 4, D](#), to segmentectomy 2 in [Figs 3, E, and 4, E](#), to segmentectomy 3 in [Figs 3, F, and 4, F](#), to segmentectomy 4 in [Figs 3, G, and 4, G](#), to left lateral sectionectomy (ie, resection of segments 2 and 3) in [Figs 3, H, and 4, H](#), and to left hepatectomy in [Figs 3, I, and 4, I](#).

Patients. The prospective database and the retrospective study were approved by our institutional review board, and patient consent was waived owing to anonymization of data in the database and its retrospective character. Patients requiring nonanatomic wedge resections were excluded from the cohort to examine only anatomic liver resections using either the intrahepatic Glissonian technique^{14,15} or standard laparoscopic technique.

Variables. Resection of ≥ 3 segments was defined as a major liver resection. The primary

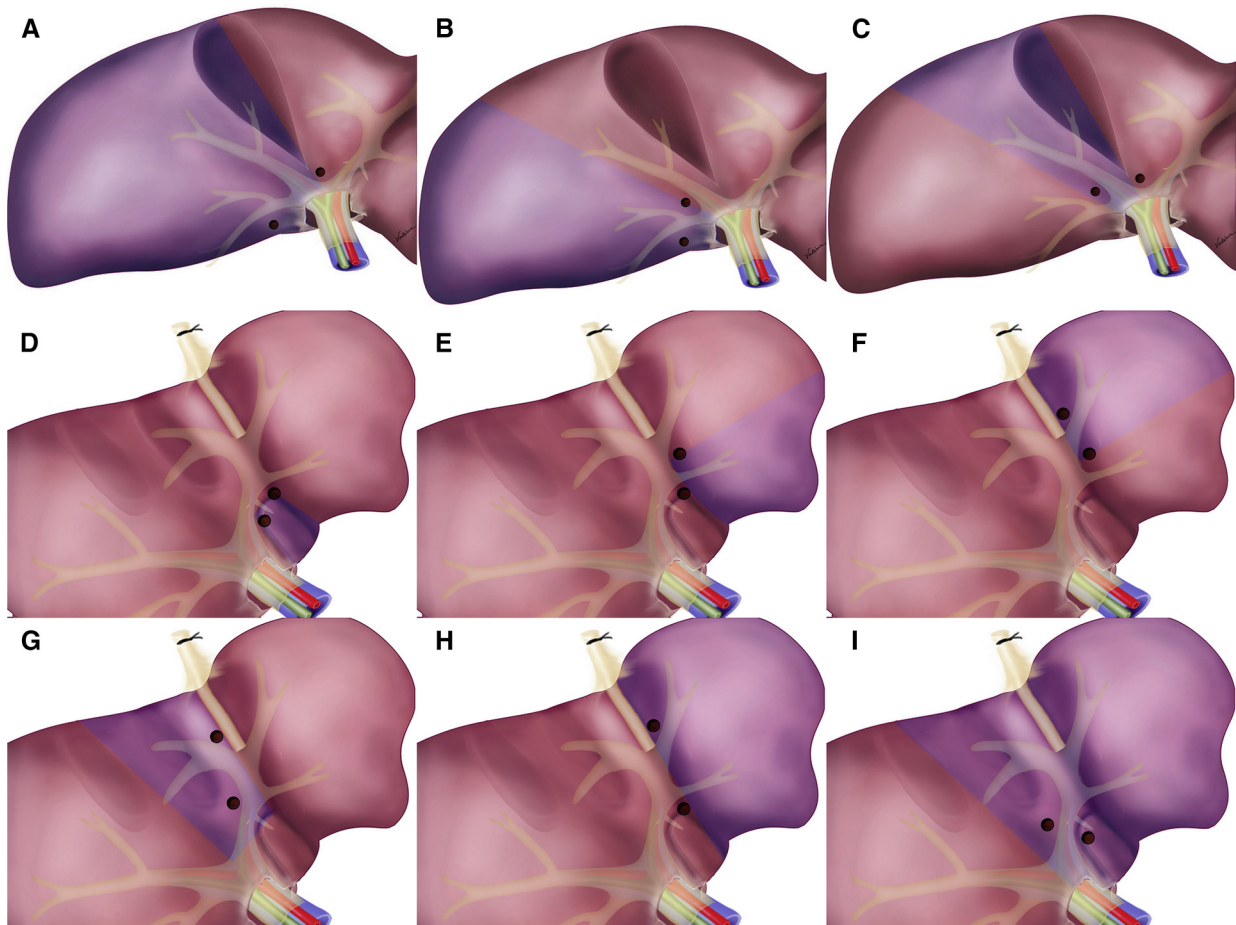


Fig 3. Diagrams of anatomic zones delineated by clamping of Glissonian pedicles for laparoscopic right and left liver resections. *A*, Right hepatectomy. *B*, Right posterior sectionectomy (segments 6 and 7). *C*, Right anterior sectionectomy (segments 5 and 8). *D*, Segmentectomy 1. *E*, Segmentectomy 2. *F*, Segmentectomy 3. *G*, Segmentectomy 4. *H*, Left lateral sectionectomy (segments 2 and 3). *I*, Left hepatectomy.

endpoint was safety of the procedures. Safety was assessed as the occurrence of complications during hospitalization. The 90-day mortality was assessed as well. To account for severity of complications, the recently published comprehensive complication index (CCI) was used.¹⁸ Secondary outcomes were the endpoints of surgical efficacy, such as conversion rates, operative times, blood loss, need for transfusions, proportion of positive margins, and duration of hospital stay.

Data sources and management. Complications were recorded prospectively by direct observation and entered into the database by residents, fellows, and clinical study nurses and double-checked in monthly research meetings dedicated to this project. A web-based calculator was used to calculate the CCI (www.assessurgery.com) in December 2014. Clinical pathology reports were reviewed to audit the database for entries on positivity of the margin in the database.

Statistical analysis. Results were reported as mean values and standard deviation for normally distributed and median values and interquartile range (IQR) for skewed data. To compare groups, the Chi-square test was used for proportions, the unpaired Student *t* test was used for parametric data, and the Mann–Whitney test for nonparametric data. The statistical analysis was performed using JMP, version 10.0.2. for Mac (SAS, Cary, NC).

RESULTS

Patients. Between 2007 and 2014, 653 liver resections were performed at our institution. Of these, 261 (40%) were performed laparoscopically, 234 of which were anatomic resections (Fig 1). The Glissonian approach was used in 114 patients and the standard laparoscopic approach in 120 (Fig 1). Usually, anatomic resection is the preferred technique whenever possible. Only 27 cases of all laparoscopic hepatectomies (10%) were

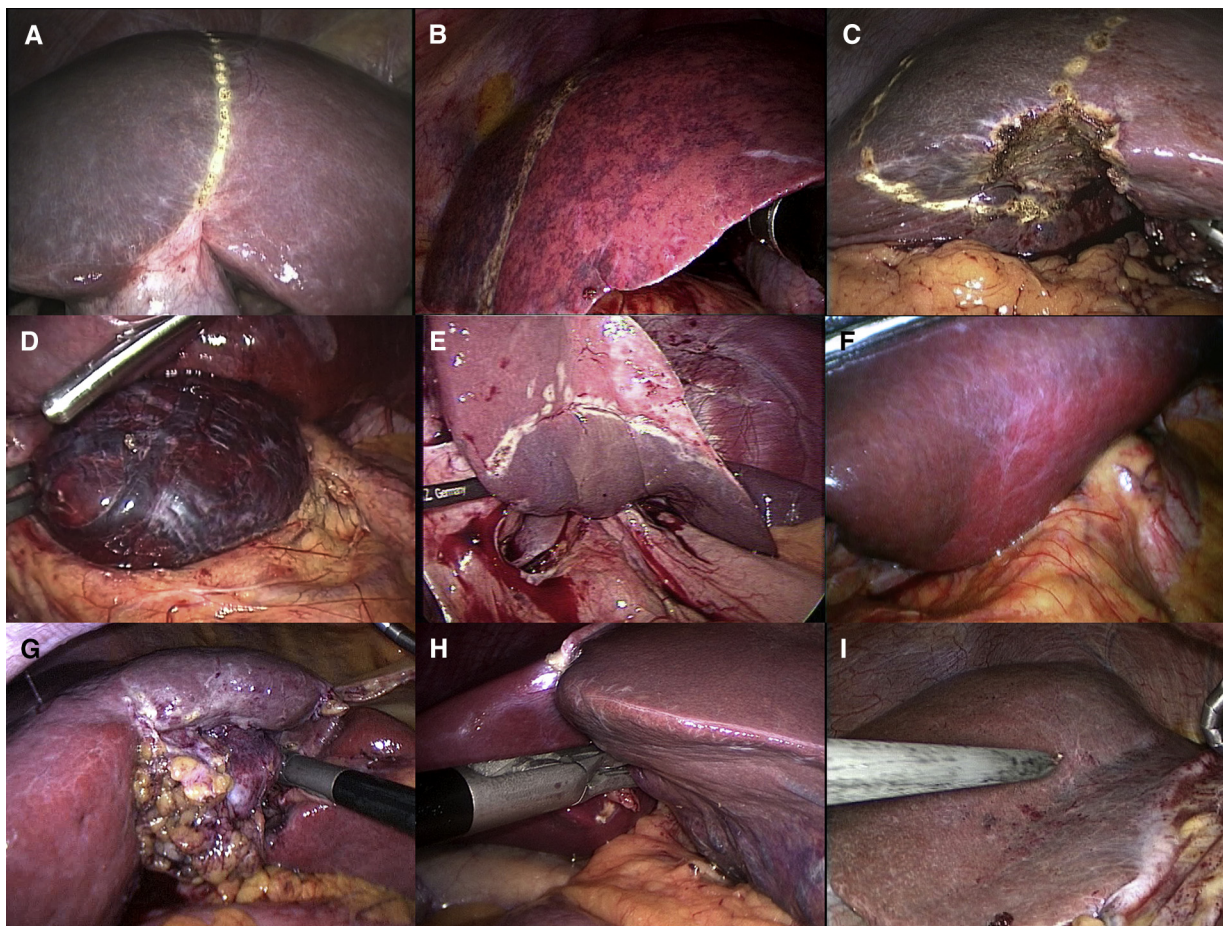


Fig 4. Intraoperative view of ischemic areas after clamping of respective Glissonian pedicles. *A*, Right hepatectomy. *B*, Right posterior sectionectomy (segments 6 and 7). *C*, Right anterior sectionectomy (segments 5 and 8). *D*, Segmentectomy 1. *E*, Segmentectomy 2. *F*, Segmentectomy 3. *G*, Segmentectomy 4. *H*, Left lateral sectionectomy (segments 2 and 3). *I*, Left hepatectomy.

nonanatomic resections and were excluded from the present study. We adopted the extra-Glissonian approach over time for many patients, because we felt it was easier, faster, and as safe and oncologically effective as the standard approach. We were able to perform segmental resections using either approach; anatomic considerations did not favor one technique over the other.

Patient characteristics. Age, sex, tumor type (metastatic vs primary), resection for malignancy, and the quality of the liver parenchymal (normal vs cirrhotic) were comparable in both groups (Table I). The number of major liver resections (resection of ≥ 3 contiguous segments) was greater in the Glissonian group ($P < .001$), and more patients were operated using the Glissonian approach in the last era of 2011–2014. The anatomic distribution of the resections is given in Table II. Bisegmentectomies of the right liver were performed more commonly using the Glissonian approach, whereas

segmentectomies of the right liver were performed more commonly using the standard conventional approach. The majority of left lateral segmentectomies were performed using the extra-Glissonian approach (Table II).

General outcomes. *Conversion to open surgery.* Two patients required conversion to an open operation in the Glissonian approach, in one owing to hemorrhage and in another owing to massive CO₂ embolism (stapler failure during division of the right hepatic vein; Table III). Five patients in the standard group underwent conversion to open surgery, 3 owing to hemorrhage, 1 owing to technical difficulties, and 1 owing to an uncertain surgical margin.

Intraoperative endpoints of safety. There was a greater proportion of patients with blood loss in range of 600–1,000 mL in the standard as compared with the Glissonian group (20 vs 7%, respectively; $P = .003$; Table III). More patients

Table I. Demographics of 234 patients undergoing laparoscopic liver resection, 2007–2014

Variable of interest	Standard (n = 120)	Glissonian (n = 114)	P value
Age, y, median (IQR)	53 (42–65)	55 (45–61)	.278
Sex, male/female, n (%)	66/54 (55/45)	60/54 (53/47)	.716
Type of operation, n (%)			<.001
Minor (<3 segments)	91 (76)	63 (55)	
Major (≥3 segments)	29 (24)	51 (45)	
Era of operation, n (%)			<.001
2007–2010	63 (52)	34 (30)	
2011–2014	57 (48)	80 (70)	
Tumor type, n (%)			.209
Primary	43 (36)	50 (44)	
Secondary	77 (64)	64 (56)	
Liver parenchyma, n (%)			.573
Normal	109 (91)	101 (89)	
Cirrhosis	11 (9)	13 (11)	

IQR, Interquartile range.

Table II. Anatomic types of 234 laparoscopic liver resections, 2007–2014

Anatomic location of resection	Standard (n = 120)	Glissonian (n = 114)
Left Liver		
Sg1	1	2
Sg2	5	1
Sg3	12	3
Sg4	6	5
Bisegmentectomy 2/3	4	40
Left hemihepatectomy	4	11
Right liver		
Bisegmentectomy 5/8	1	3
Bisegmentectomy 6/7	3	9
Bisegmentectomy 7/8	3	—
Sg5	15	—
Sg6	21	—
Sg7	6	—
Sg8	9	—
Right hemihepatectomy	23	32
Bilateral		
Right trisectionectomy	1	5
Mesohepatectomy (Sg 4/5/8)	1	3
S4b-S5	5	—

Sg, Segment.

required blood transfusion in the standard group compared with the Glissonian group respectively (19 vs 13% respectively; $P = .213$). The mean operative time in the standard group was greater as compared with the Glissonian group (245 ± 123 vs 139 ± 75 minutes, respectively; $P < .001$).

Surgical margins. Three patients operated on for malignant disease in the control group had positive margins. There were no positive margins in the Glissonian group (Table III).

Hospital stay. Patients in the Glissonian group had a lesser median hospital stay of 2 days (IQR, 1–4) versus 4 (IQR, 2–5; Table III).

Safety outcomes. Overall complications occurred in 58% of the patients in the standard group compared with 44% of the patients in the Glissonian group ($P = .037$). One patient in each group died postoperatively, resulting in a 90-day mortality of 1% in both groups ($P = .971$; Table IV). The median CCI was 20.9 (IQR, 8.7–20.9) in the standard group compared with 8.7 (IQR, 0–20.9) in the Glissonian group ($P = .001$). The respective linear models showed a decrease in CCI over time, potentially an effect of learning to perform laparoscopic resections (Fig 5).

DISCUSSION

A retrospective study in patients with hepatocellular carcinoma demonstrated that the Glissonian approach was an independent prognostic indicator for survival over the standard approach in open liver surgery.¹⁹ A prospective, randomized study showed that the Glissonian approach was faster than hilar dissection.²⁰ Our study is the first comparison between the Glissonian and the standard approach in laparoscopic surgery. It shows that the safety concerns raised by critics against the laparoscopic Glissonian are not justified, specifically not as far as the risk of bile duct injury is concerned. Although only one 90-day mortality occurred with each technique in the 234 patients, we found fewer overall complications and a lesser CCI in the Glissonian group compared with the standard approach. But there remains the important limitation of this study in that a substantial proportion of patients from Glissonian group were operated during the

Table III. General outcomes of 234 patients undergoing laparoscopic liver resection, 2007–2014

Variable of interest	Standard (n = 120)	Glissonian (n = 114)	P value
Operative time, min, mean (SD)	245 (123)	139 (75)	<.001
Patients transfused (RBC), n (%)	23 (19)	15 (13)	.213
Blood loss (mL), n (%)			.011
<100	66 (55)	83 (73)	.046
101–600	25 (21)	18 (16)	.319
601–1,000	24 (20)	8 (7)	.003
>1,000	5 (4)	5 (4)	.933
Conversion, n (%)	5 (4)	2 (2)	.278
Hospital stay, d, median (IQR)	4 (2–5)	2 (1–4)	<.001
Malignant tumor in pathology, n (%)	90 (75)	84 (74)	.817
Positive microscopic margins, n (%)	3 (3)	0 (0)	<.001

IQR, Interquartile range; RBC, red blood cells; SD, standard deviation.

Table IV. Complication outcomes of 234 patients after laparoscopic liver resections, 2007–2014

Variable of interest	Standard (n = 120)	Glissonian (n = 114)	P value
90-day mortality, n (%)	1 (0.8)	1 (0.9)	.971
Overall complications, n (%)	69 (58)	50 (44)	.037
CCI, median (IQR)	20.9 (8.7–20.9)	8.7 (0–20.9)	.001
Cirrhotic patients with complications	8/11	3/13	—

CCI, Comprehensive complications index; IQR, interquartile range; SD, standard deviation.

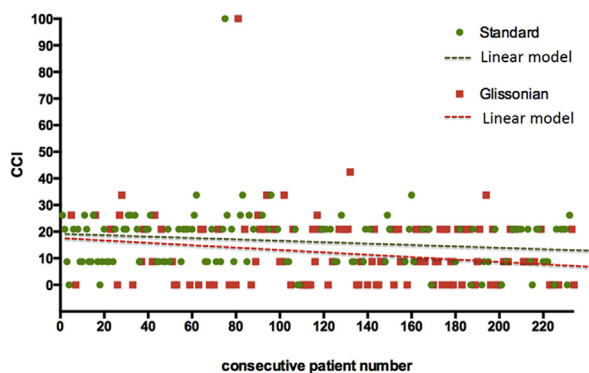


Fig 5. Comprehensive complication index (CCI) of all consecutive laparoscopic liver resections performed by standard and Glissonian approach between 2007 and 2014. The respective linear models show a slight decrease in CCI over time, which may be an effect of learning to perform laparoscopic resections.

later time period, and improved results we noted may well be related to a learning curve in the laparoscopic approach overall.

Although the Glissonian approach has only been accepted with hesitation owing to concerns about stapling the Glissonian pedicles intrahepatically, this study shows for the first time that these concerns cannot be substantiated in a single center that has extensive experience with this approach.

Because this study is a retrospective audit of a prospectively maintained database, the decision by surgeons to use the Glissonian instead of the standard approach may involve a number of biases, which we tried to lay open and address. After 7 years of experience, we conclude for our practice that segmental resections should be performed preferentially using the Glissonian approach owing to the ease of following the lines of vascular demarcation during the parenchymal transection. At the same time, we believe that there remains a certain equipoise in right and left hepatectomies, whether the Glissonian or standard approach should be used. We choose to use the recently upgraded scoring system, the CCI, as a safety outcome, because it assesses all complications, not just the most severe, and allows the expression of complications on a scale of 1–100.¹⁸ Both operating time as well as blood transfusion have to be considered markers of the physiologic severity of liver resection. Studies have demonstrated the correlation of increased operating time and blood transfusions with increased complication rates in complex open liver surgery,^{21,22} and the same seems to be true for laparoscopic liver surgery in this study. The Glissonian approach, possibly owing to its simplicity and the strategy of strict anatomic demarcation before parenchymal

transection, may be less demanding physiologically for patients. Additionally, the early discontinuation of inflow makes the potential use of the Pringle maneuver pointless in most cases and thereby, decreases a fundamentally unnecessary ischemia/reperfusion injury to the entire liver.

Anatomic removal of liver segments may well be accomplished laparoscopically without the Glissonian approach,⁸ but ischemic delineation of single segments is only possible by accessing the secondary bifurcation, which is located intrahepatically and not accessible through a hilar approach. All other segmental variations require the use of anatomic approximation or the use of laparoscopic ultrasonography with extrapolation of resection lines and, therefore, there is a risk of ischemic remnants owing to incorrect mapping. In contrast, the Glissonian approach allows for straightforward control of Glissonian sectional pedicles beyond the primary bifurcation and also avoids any hilar dissection.^{14,15} The Glissonian pedicle may be clamped with small incisions at specific anatomic landmarks, allowing a precise ischemic delineation of the only segments to be resected. It is important to note that the anatomic parameters related to the intrahepatic Glissonian approach do not vary by sex or liver weight. No substantial difference was observed in these and other parameters in a recently published anatomic study.²³

In some situations, when segmental demarcation is not convincing, repeat clamping may be attempted until the desired demarcation is achieved. Bleeding from these incisions is minimal, and inflow is stopped after stapling the pedicles. The Glissonian technique in laparoscopy can be used to perform not only major hepatic resections, but also anatomically tailored monosegmentectomies or bisegmentectomies, which allows parenchymal-sparing resections by virtue of its anatomic precision in the field of laparoscopic liver surgery which has been accused of underusing selective resections. Additionally, the better delineation of segmental borders may avoid partially ischemic and nonfunctional remnants, which may be a source of infection and necrosis. All these factors may explain the apparent decrease in overall complication rate we found in this study.

The nonanatomic approach in open liver surgery has been associated with high rates of margin positivity in the literature of between 16% and 35%.^{24,25} In our study, margin positivity was quite low overall and, thus, we conclude that there is no oncologic concern based on the evidence from 114 patients using standard histologic evaluation.

The Glissonian approach may well be extended to patients with underlining chronic liver disease and cirrhosis.^{26,27} Twenty-four patients with cirrhosis were included in this study. Although no conclusion should be drawn from this small number of patients, the Glissonian approach may actually have resulted in fewer complications (3/13 patients) in cirrhotic patients compared with the standard laparoscopic approach (8/11 patients).

During the recent consensus conference of laparoscopic liver surgery in Morioka,²⁸ it was emphasized that the extra-Glissonian approach requires specific proctoring to ensure knowledge of anatomic landmarks and the correct use of the small incisions to retrieve the pedicles inside the liver parenchyma. The Glissonian approach in open surgery requires an insertion of a right-angle instrument or an atraumatic retriever around the pedicles.²⁹ Of course, this maneuver has to be modified by the laparoscopic surgeon. We would like to emphasize, however, that all of laparoscopic liver surgery requires specific knowledge of anatomy, selected instruments, and certain maneuvers. Every novel approach will result in a learning curve and may require proctoring by experienced surgeons, when the extra-Glissonian approach is first used. For some surgeons, intraoperative ultrasonography may be used to ascertain the localization of the pedicles, making the insertion of the vascular clamp safer. Others may prefer to define the correct position of the clamp by cholangiography.³⁰ More recently, some authors are using special instruments to encircle the pedicle, thus avoiding blind stapling of the pedicle and again others are dividing the Glissonian pedicle after the transection of the liver parenchyma to ensure the correct position of the stapler.^{31,32} In some cases, it was possible to actually encircle the pedicle with the use of some special instruments.²⁹ It may be of particular importance in right hemihepatectomy, where the main bile duct runs close to the bifurcation; this is important because, if appropriate attention is not paid during this maneuver, injury to the bile duct can occur. In our experience with the open and laparoscopic Glissonian approaches, we had no case with such a bile duct injury. Our experience with simple intrahepatic stapling after tentative clamping has been very rewarding. As with any mature laparoscopic procedure, the Glissonian approach allows for many such variations without losing its fundamental advantage of anatomic ischemic delineation of the part of the liver to be resected.

In conclusion, this observational study did not confirm concerns about a lack of safety of the

laparoscopic Glissonian approach. Although these results could be related to an ongoing learning curve in the practice of laparoscopy overall, we observed less complications, lesser operative times, and less blood loss comparing the Glissonian approach to standard laparoscopic liver resections.

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