Asian Journal of Surgery 44 (2021) 147–152

Contents lists available at ScienceDirect

Asian Journal of Surgery

journal homepage: www.e-asianjournalsurgery.com

Original Article

The role of Intraoperative cholangiography (IOC) and methylene blue tests in reducing bile leakage after living donor hepatectomy☆

Umut Tuysuz [a,*], Hıkmet Aktas [b], Imam Bakır Batı [b], Remzi Emıroglu [b]

[a] Departman of Hepatopancreatobiliary Surgery, Şişli Etfal Hamidiye Training and Research Hospital, İstanbul, Turkey
[b] Departman of Transplant Surgery, Faculty of Medicine, Acıbadem Unıversity, İstanbul, Turkey

ARTICLE INFO

Article history:
Received 19 December 2019
Received in revised form
18 March 2020
Accepted 20 April 2020
Available online 14 August 2020

Keywords:
Bile leakage
Donor
Living donor liver transplantation
Intraoperative cholangiography test
Methylene blue test

ABSTRACT

Aim: Liver transplantation remains the only curative treatment in end stage liver disease. Biliary complications remain the most common major morbidity causes in hepatic resection. We aimed to determine and eliminate the bile leakage in donor hepatectomy of LDLT.
Material and methods: This study was conducted retrospective and one center study. The study population included 110 consequential liver donors with major liver resection (more than three segments). The population was divided into three groups for data analyses. Primary study groups included 40 donors subjected to methylene blue test starting in April 2013 and 40 donors subjected to intraoperative cholangiography started in March 2014.
Results: A total of 110 liver donors (42.7% women) were included in the study. Postoperative biliary complications were less in methylene blue and intraoperative cholangiography (IOC) groups. Bile leakage was significantly higher in control group (23.3%) compared to methylene blue (5%) and IOC groups (2%) Average duration of hospital stay and duration of operation were significantly higher in control group compared to methylene blue and IOC groups.
Conclusion: In our study we conducted to establish biliary leakage in living donor hepatectomy which intraoperative cholangiography test was used to determine. Many intraoperative methods have been introduced to prevent biliary leakage and development of complications. We have showed that IOC test used in the present study could be easily applied in both living liver donor hepatectomy and other major hepatectomy cases. IOC test reduced postoperative biliary leakage incidence and did not increase incidence of other complications.

1. Introduction

Liver transplantation remains the only curative treatment in end stage liver disease. In the case of limited available deceased organ donors, living donor liver transplantation (LDLT) becomes an attractive way of organ availability. LDLT has excellent recipient outcomes, thereby reducing waiting list mortality.[1] LDLT is less common, and since there is a risk of this procedure for donors, the safety of liver donor is the most important concern. LDLT has an estimated donor mortality of 0.1–1%.[2] Recipient mortality, on the other hand, varies widely and can reach up to 60%. The most frequent reasons for morbidity after liver donation are infections and biliary complications. The adult living donor liver transplantation cohort study (A2ALL), the largest outcome study of LDLT donors in the US, reported an overall donor morbidity of 38%. Biliary leakage constituted 9% of all complications. Advances in surgical procedures and better understanding of liver anatomy and physiology have decreased post-operative hepatic failure and the need for intraoperative blood transfusionin major liver resections carried out for any causes. Nevertheless, these advances have not improved post-operative biliary leakage and this problem continues to be the Achilles' heel of liver resection.[3–9] Along with the advances in perioperative care and surgical procedures, postoperative morbidity and mortality have been decreased prominently. However, incidence rate of biliary leakage has not changed much in the last a few decades. In recent studies, incidence rates from 4.0 to 9.8% have been reported.[10–15] Biliary complications

☆ Using tests for reducing bile leakage after LDLT donor hepatectomies.
* Corresponding author. 2123386300, Istanbul, Turkey.
E-mail address: umutuysuz@gmail.com (U. Tuysuz).

https://doi.org/10.1016/j.asjsur.2020.04.001
1015-9584/

remain the most common major morbidity causes in hepatic resection.[10] Bile presence in peritoneal cavity could be eliminated by regular body defense mechanisms. However, it predisposes for the development of liver failure, sepsis and mortality.[11,12] Thus, many methods have been described to prevent biliary leakage after liver transection such as staining of liver surface subjected to transection with fibrin glue, determination of orifices in bile ducts using air injection under ultrasound imaging and intraoperative cholangiography.[16] Although postoperative biliary leakage was controlled by drainage and use of antibiotics in many cases, these procedures are costly and require longer hospital stays. In addition, biliary leakage after hepatic resection could lead to systemic morbidity cascade in some cases resulting from intra-abdominal sepsis. Secondary complications related to biliary leakage could result in more invasive procedures such as venous thromboembolism and relaparotomy and mortality increase.[15,17,18]

As a strategy to decrease postoperative biliary leakage, a catheter is advanced into main bile duct through ductus sisticus after cholecystectomy and liver resection, and distal choledochus is occluded. A solution such as oil emulsion, isotonic sodium, indocyanine green or methylene blue is slowly injected into biliary tree and presence of biliary leakage in transected liver surface can be determined. Some studies using this technique could determine leakage points intra-operatively in 19.7–80.8% of the patients.[11,19–22] Several studies showed the usefulness of biliary leakage test in prevention of postoperative biliary leakage. However, some other studies did not find any benefit of using this test. In addition, procedures involving this test could lead to complications. Some studies showed that excess bile pressure caused by biliary leakage test could cause cholangitis and cholangiovenous reflux.[23,24] No standard method has been defined for the prevention of postoperative biliary leakage. The present study was carried out to determine the systemic benefit of organizing intraoperative methylene blue and intraoperative cholangiography to detect and repair the open biliary ducts. Postoperative biliary leakage rate was decreased. Therefore, using the above mentioned results, we aimed to determine and eliminate the bile leakage in donor hepatectomy of LDLT.

2. Material and methods

The study population included 110 consequential liver donors with selected major liver resection (more than three segments). The population was divided into three groups for data analyses. Primary study groups included 40 donors subjected to methylene blue test starting in April 2013 and 40 donors subjected to intraoperative cholangiography started in March 2014. Acıbadem hospital is annually performs more than one hundred liver transplants, which gave us one of the largest data sets regarding liver transplantation in Turkey. More than % 95 of liver transplants are living donor liver transplantation in our instution. These groups included all living donor hepatectomies in a single center for whom the method was used excluding the ones operated during learning curve. A third group consisted of patients operated in the period preceding intraoperative cholangiography and methylene blue test.

2.1. Preoperative evaluation

Preoperative evaluation included high resolution computed tomography (3–5 ml/s rapid intravenous contrast matter injection, three phase and 2.5–5.0 mm sections along the liver) and/or contrast agents and magnetic resonance imaging used in liver protocol. The remaining liver volume was calculated as previously described. If the remaining liver volume was not sufficient, operation was abandoned.

2.2. Surgery

First, preoperative ultrasound examination (5–7.5 MHz probe) was performed to visualize biliary structures, to determine of appropriate transection plane and reveal associations between transection plane and vascular bile ducts. Parenchymal transection method was decided by surgeon based on the condition of liver parenchyma. All cases were operated using two-surgeon method in which saline-linked cautery (the second surgeon) and ultrasonic dissector (the first surgeon) combination was employed. During liver resection, biliary ducts and larger veins were closed through suture ligation or absorbable clips. Resection was carried out using continuous irrigation and bipolar forceps along with ultrasonic dissector and similar methods. Closing of total or selective hepatic flow (Pringle maneuver) were performed in most cases for periods varying from 5 to 15 min. The first evaluation of transection surfaces in all three groups were carried out by direct vision of open ducts and by white compress. Transection surfaces were closed using polypropylene suture.

2.3. Methylene blue test

Except for patients who had cholecystectomy before, after ensuring homeostasis and after closing all biliary leakages on transection surface which were detected by white gas, a disposable cholangiography catheter was advanced into ductus sisticus and fixed using a silk suture. Methylene blue solution was slowly injected into biliary tree and distal common bile duct was simultaneously closed with a finger. Defective ducts were determined through observing the leakage of methylene blue solution via open bile ducts on transected liver surface. These ducts were instantly closed with suture or clips. Liver surface was washed using sterile isotonic. Then, the procedure was repeated until no methylene blue solution was observed on liver surface.

2.4. Intraoperative cholangiography test

As explained earlier, a 4-ft cholangiography catheter was advanced into ductus sisticus and fixed using a silk suture. Five to ten ml of contrast matter (meglumine diatrizoate, 76% 100 ml diluted byphysiological saline as 1:1) was slowly injected into biliary tree. At the same time, distal common bile duct was occluded with a finger. Then, during breath holding moment of the donor, posteroanterior images were obtained digitally. Bile duct leakages on liver surface and at hepatic influence level was determined digitally in the form of contrast matter extravasation. Leaking ducts were repaired, and the procedure was repeated until no contrast matter extravasation was observed.

2.5. Post-operative results, data collection and description

The Clavien–Dindo classification is applied to evaluate postoperative complications and consists of 7 grades (I, II, IIIa, IIIb, IVa, IVb, and V); this classification is valid and applicable worldwide in many fields of surgery [25]. In general, each complication has a corresponding grade, and the final grade of complications is adopted the highest. Hospital stays were calculated as the number of days from operation to hospital discharge. Post-operative mortality included the time period 90 days after the operation. Drain placement was performed when considered necessary by surgery team. When the liquid coming to drainage was not purulent or without bile, drain was pulled off before the discharge of patient. When the bilirubin amount in drainage liquid was the same as serum bilirubin concentration on post-operative three days or at least for three times, it was considered a biliary leakage. This analysis was performed only when there was a biliary leakage suspicion. Similarly, peritonitis indicating clinically important biliary leakage was measured when suspicious radiological findings were present. After operation, 11 patients (no test group; 30/7, methylene blue group; 40/2, IOC group; 40/2) had short-term perioperative complications. Followed by the Clavien–Dindo classification, 9 patients presented with grade I complications (with bile leakage) and 2 patients exhibited grade II complications (1 patient with bile leakage, 1 with delayed wound healing). Post-operative serum ALT, AST, direct and indirect bilirubin levels were routinely measured in all patients as indications of biliary leakage and related complications. Patient demographics included types of variation in biliary anatomy. No test group had 10 patients who abnormal anatomy (9 patients two orifices, 2 patients three orifices), methylene blue group had 24 patients who abnormal anatomy (21 patients two orifices, 3 patients three orifices), IOC group had 22 patients who abnormal anatomy (20 patients two orifices, 2 patients three orifices).

2.6. Statistical analyses

Statistical analyses were performed using SPSS software (Version 22.0). As the descriptive statistics of data, mean, standard deviation, median, minimum, maximum, frequency and ratio values were used. Distribution of variables were measured using Kolmogorov–Smirnov test. Kruskal–Wallis and Mann–Whitney U test were used for the analyses of independent quantitative variables. For qualitative data, chi-square test was used when appropriate. When the conditions were not met for Chi-square test, Fischer test was used for the same purpose.

3. Results

Sixty-three of the donors were male (57.3%) and fourty seven were women (42.7%). Median age in control group, methylene blue and IOC test groups was 33.5 years (range: 20–47). Living donor right hepatectomy was performed in all patients. At least one biliary leakage was observed and repaired during intraoperative examination in 15 patients (13.6%). No patients had any major complications. There were no significant differences among groups for clinicopathological characteristics. Age, gender distribution and liver parenchyma characteristics were similar in all three groups. In terms of intraoperative characteristics, no difference was observed among the study groups except for twice higher contrast matter detection and repair in methylene blue test groups compared to IOC test group. Post-operative biliary complications, on the other hand, were less in methylene blue and IOC groups. Bile leakage (grade 1 and 2) was significantly higher in control group (23.3%) compared to methylene blue (5%) and IOC groups (5%) ($p < 0.05$). Difference between methylene blue and IOC groups for bile leakage was not significant. Average duration of hospital stay and duration of operation were significantly higher in control group compared to methylene blue and IOC groups ($p < 0.05$). However, the differences between methylene blue and IOC groups for duration of hospital stays and duration of operation were not significant. Serum direct bilirubin levels were not significantly different between control and methylene blue groups. However, control and methylene blue groups had significantly higher direct bilirubin levels compared to IOC group ($p < 0.05$). On the other hand, the difference between methylene blue and IOC groups was not significant. No differences were observed among three study groups for ALT and total bilirubin levels(Table 1).

4. Discussion

Post-operative biliary complications still remain a major problem in liver surgery. As in other major hepatectomies performed due to various reasons, the most common post-operative complication in living liver donors is biliary complications[26] and they have considerable postoperative effects on life quality of liver donors such as abdominal infection and liver failure. Multiple strategies have been employed to decrease these complications. However, along with the increases in liver surgery, mortality due to these complications are also on rise. Because of insufficiency of cadaver pool for liver transplantation, living donor hepatectomy frequency is increasing. Most of the studies focused on biliary complications in recipient outcomes of LDLT follow-ups. Only six studies from 2006 to 2015 dealt with living donor complications. A study from a single center in Japan[27] reported a biliary complication incidence frequency of 7.5% in 731 donor hepatectomy patients in 1999–2006 period. Most of those complications were associated with biliary leakage. Incidence rate of biliary leakage was 9.9–11.1% in donors subjected to right hepatectomy. As a result of these complications, endoscopic retrograde cholangiopancreatography (ERCP) was performed on 29 patients and six patients were operated. In another study dealing with biliary complications of 207 patients who had right hepatectomy in an Egyptian transplantation center from 2001 to 2008, a 13% incidence rate was calculated for biliary complications.[28] A biliary complication incidence rate of 4.1% ($n = 14$) was reported for 343 donor hepatectomy cases (210 left liver and 106 right liver) by a study conducted in Japan in 1996–2009 period.[29] Shin et al (2012) carried out another study in Japan during 1996–2011 period on 827 living donor hepatectomy patients from a single center.[30] A great majority of the patients had right hepatectomy and complication rate was 10.0%. About one out of five complications (19.8%) involved biliary complications. Another Egyptian study published in 2014 reported a biliary complication rate of 11.1% in 216 living donors who had right hepatectomy from 2004 to 2013.[31] A recent study from Turkey found a biliary leakage incidence of 7.7% for 593 living donors operated between 2006 and 2012.[32] Thus, it could be stated that biliary complication rate ranges from 2 to 18%.

Great majority of biliary complications are biliomas and bile leakages, could be improved without using ERCP or percutaneous drainage. Strictures are less frequently observed and are generally fixed by ERCP and stent placement. More serious complications involving biliary tree injury or refractory bile leakages from dissected surfaces call for operative intervention. About 9% of biliary complications need subsequent surgical intervention. Many intraoperative methods have been introduced to prevent biliary leakage and development of complications. We have showed that the method used in the present study could be easily applied in both living liver donor hepatectomy and other major hepatectomy cases performed due to various reasons since it has data homogeneity which gives more accurate results. Determination of biliary leakage using traditional methods such as intra-operational gas test is difficult for surgeon. Hepatic resection technique necessitates biliary leakage to be minimal during the operation. Complications involving biliary leakage is undesirable in living donor hepatectomy. There has been little improvement in decreasing the post-operative biliary leakage. In a recent study, use of IOC has been introduced to determine open bile ducts which cannot be easily observed in liver transection surface, and to perform intraoperative repairing of hidden biliary fistulas. More importantly, systemic benefit of IOC was its association with lower incidence and severity of post-operative biliary complications. In a multivariable analysis, this independent variable was found to be the most significant risk factor in patients suffering from post-operative biliary leakage. IOC

Table 1

With Biliary Compication				Without Biliary Complication			
Postop.AST	Postop.ALT	Postop.D.Bil	Postop.T.Bil	Postop.AST	Postop.ALT	Postop.D.Bil	Postop.T.Bil
298	242	1.37	3.02	263	330	1.01	2,2
592	390	1.46	2.41	107	74	0.8	2.29
158	128	0.67	1.64	505	564	1,0	2.17
254	267	1.05	1.87	318	632	0.37	0.9
409	420	0.68	1.74	575	390	0.78	1.75
233	205	0.69	1.55	456	300	0.82	2.08
433	379	0.62	0.96	337	337	0.72	1.68
				346	348	0.71	2.07
				232	248	0.84	2.21
				225	230	0.48	1.29
				151	192	0.62	1.72
				158	111	0.58	2.6
				230	288	0.39	0.95
				214	179	0.45	0.91
				211	238	1.92	6.96
				348	315	1.03	3.01
				119	138	1.01	2.06
				271	356	0.54	1.18
				192	108	0.54	1.13
				96	85	0.81	1.38
				271	266	0.68	1.92
				349	226	0.62	1.4
				325	270	0.87	1.76

With Biliary Compication				Without Biliary Complication			
Postop.AST	Postop.ALT	Postop.D.Bil	Postop.T.Bil	Postop.AST	Postop.ALT	Postop.D.Bil	Postop.T.Bil
357	375	0.9	1.7	96	85	0.81	1.38
1070	908	2.6	4.5	271	266	0.68	1.92
				349	226	0.62	1.4
				325	270	0.87	1.76
				398	358	1.27	2.48
				405	368	0.61	1.48
				493	360	1.19	2.38
				319	230	0.71	1.38
				383	368	0.62	1.58
				234	50	0.72	1.54
				494	466	0.5	0.97
				464	331	0.72	1.31
				466	565	0.84	1.83
				346	269	0.62	1.27
				264	190	0.74	1.86
				265	267	0.3	0.7
				531	668	1.1	2.2
				397	230	1.8	2.9
				647	527	1.7	3.9
				277	218	0.6	1.3
				512	605	1.7	2.8
				249	283	0.6	2.3
				267	242	0.7	1.5
				390	360	1.3	3.1
				255	135	0.5	1.1
				664	563	1,0	2,0
				438	282	0.8	1.4
				365	371	0.5	1,0
				272	239	1.1	3.4
				292	187	0.7	1.2
				747	439	1.2	2,0
				457	291	0.5	1.5
				590	562	1,0	3.5
				474	301	0.5	1.2
				293	189	0.6	1.4
				210	143	0.9	1.9
				502	283	1.2	2.7
				440	272	0.8	1.7

İNTRAOPERATİVE CHOLANGİOGRAFİ

With Biliary Compication				Without Biliary Complication			
Postop.AST	Postop.ALT	Postop.D.Bil	Postop.T.Bil	Postop.AST	Postop.ALT	Postop.D.Bil	Postop.T.Bil
321	258	0.9	1.7	289	189	0.5	1.1
488	391	0.7	1.4	354	308	1.1	2.7
				286	205	0.9	1.6
				225	174	0.7	4.6
				447	157	0.7	1.6
				274	313	1.7	3.6

Table 1 (*continued*)

With Biliary Compication				Without Biliary Complication			
Postop.AST	Postop.ALT	Postop.D.Bil	Postop.T.Bil	Postop.AST	Postop.ALT	Postop.D.Bil	Postop.T.Bil
				283	192	0.6	1.7
				680	579	1.3	2.9
				517	355	0.6	1.7
				285	259	0.9	1.8
				685	667	0.6	1.5
				323	220	0.5	1.3
				581	427	0.7	1.7
				311	229	0.4	1.2
				634	484	1,0	2.1
				448	368	0.7	1.7
				317	278	0.3	0.9
				314	287	0.4	1.1
				88	58	0.3	0.7
				563	281	0.6	1.6
				314	452	0.5	2.2
				350	346	0.6	2
				397	350	0.5	1.7
				213	146	0.3	0.9
				573	402	0.5	1.3
				281	241	0.5	2.2
				112	88	0.5	1.4
				671	560	0.6	1.3
				332	263	0.4	1.5
				310	297	0.7	1.7
				421	572	0.5	2.1
				530	446	0.9	2.3
				173	199	0.2	0.9
				412	251	0.7	1.5
				382	366	0.3	3.7
				438	350	0.6	3.9
				423	342	0.3	1.3
				410	330	0.2	0.4

provided live donor hepatectomy surgeons with a cost-effective, reliable, practical method with minimum biliary leakage sequel and incidence after hepatectomy. The aim of the biliary leakage test was to determine insufficiently closed bile duct orifices in liver transection surface and subsequent suturing of leaking area.[33] A recent study reported increasing biliary leakage along with increasing complex hepatectomy. This difference in biliary leakage rate continued in patients who had biliary enteric anastomosis, which in fact was significant considering only the patients with major hepatectomy. We also observed such an increase in living donor hepatectomy patients and it became a focus of necessity for clinical practice. Live donors in the present study had post-operative biliary leakage risk, and intraoperative determination of open biliary ducts could be useful for them. In addition, homogeneous and healthy individuals in the present study reflected the reliability and usefulness of leakage test used to prevent post-operative bile leakage. It seems that this method could also be used for liver resections performed due to other causes (hepatobiliary tumors, giant hemangiomas, etc.).

A meta-analysis showed that biliary leakage test group had less leakage than non-biliary leakage test group. This test was shown to be effective and reliable in determining the postoperative bile leakage. Although not widely accepted, several methods were proposed to detect biliary leakage in the past decade. Intraductal saline injection is a low cost, repeatable method. However, this method which uses a transparent solution is not satisfactory for determination of small ducts.[34] Injection of a colored solution (methylene blue or indocyanine green) was proposed.[7,11,18,35] However, in order for these solution to allow imaging of leakage area, they need to be darkened. This approach has disadvantages of masking of small open ducts along with the coloring of transection surface, and difficulty of cleaning the dye from the surface, which makes subsequent repeating of the test to determine leakage difficult. We experienced these difficulties in methylene test group. Determination of bile leakage and repair were performed in five donors in methylene blue test group, while bile leakage test and repair were performed in 10 donors in IOC test group (25%). There was no difference for post-operative bile leakage between the two groups. In a study where indocyanine green was used, ICG was injected into the bile duct, and bound the protein in bile. Fluorescent imaging was used to monitor bile-ICG mixture with an infrared camera. Biliary leakage was searched through extra biliary fluorescence signals.[33,36,37] However, no association was found between biliary leakage incidence and post-operative complications. Besides, this method requires longer time, specialized equipment, shutting down of the lights in operation room and a complex algorithm to determine open biliary ducts indirectly on a monitor. All these considerations compromise the usefulness of the method. 'White test' based on intraductal injection of a 5% oil emulsion can be employed. This was reported to be a sensitive and low-cost repeatable method by a study with limited number of patients in which 25 patients were subjected to biliary duct resection and biliary enteric anastomosis.[33] That study compared white test with saline test and concluded that the former was superior. Resection area was not contaminated and was easily washed, and the test could be repeated.[33] Furthermore, oil emission involved foreign cells and its intraductal injection could lead to allergic reaction, oil embolism, immunosuppressive effect and fungal infections. Alt test which employs air to detect biliary leakage was reported to be advantageous in that it needs no extra technology, it has a shorter learning curve, it is repeatable and it does not lead to staining of resection surface. That study found a postoperative biliary leakage rate of 1.9%. Biliary leakage incidence in the present study was similar. However, it resulted in negative alt in patients who had anatomic variations of common bile duct and lower cystic confluence. In addition, patients who underwent liver resection in that study were quite heterogeneous for indications. On the other hand, the present study included only healthy and homogeneous living donor patients who were relatively younger. Therefore, patient related factors did not affect the test outcomes in the present study. In addition, when a very high biliary duct pressure is induced, biliary leakages may not be observed during the operation.[11] Small bile ducts on the surface of liver can be obstructed by microliths[12] and bile leakages in this area may not be observed through air test. Bile leakages may arise when microliths fall after operation. On the other hand, it was possible to drop microliths via liquid pressure of contrast matter in the present study and open ducts were determined. In this context, through the use of inexpensive and similar solutions via diluting and frequent use, IOC can overcome many disadvantages here. It does not involve staining of surgical area, and therefore, it can be repeated. Since contrast matter has no negative effects on patients, this method is extremely safe for patients. We did not experience technical failure with IOC. The procedure does not increase length of operation. Rather, it shortens the total operation time. Significant decreases in post-operative biliary leakages helped meeting the study aims. The number of open bile ducts determined and repaired intra-operatively was twice compared to methylene blue test. In addition, effect and safety of biliary leakage test was determined conclusively for living donors undergoing hepatectomy. Four patients occurred to be biliary leakage in methylene blue and IOC test groups. İt may be on the transected liver surface. We have determined the use of IOC and methylene blue tests as useful and have been using routinely since 2014. This study had some limitations. İt had retrospective nature and a single center study. IOC needs radiographic machine and the risk of radioactivity if repeated test is needed. To overcome these limitations, more RCTs should be conducted with large numbers of patients to achieve a sufficient level of statistical power for accurate evaluation of the bile leakage test. Based on the evidence obtained in the present study, it was concluded that IOC test reduced postoperative biliary leakage incidence and did not increase incidence of other complications. IOC could be test of choice to detect biliary leakage in major hepatectomies performed in living donors and for other reasons. İntraoperative cholangiography with either radio-opaque contrast medium or colored dye is benificial to reduce bile leak during live donor major hepatectomy.

Declaration of competing interest

All of the authors (U. Tuysuz,H.Aktas,I.B.Batı and R. Emıroglu) have declaration of any potential financial and non-financial conflicts of interest.

References

1. Olthoff KM, Smith AR, Abecassis M, et al. Defining long-term outcomes with living donor liver transplantation in North America. *Ann Surg*. 2015;262: 465–475.
2. Roll GR, Parekh JR, Parker WF, et al. Left hepatectomy versus right hepatectomy for living donor liver transplantation: shifting the risk from the donor to the recipient. *Liver Transplant*. 2013;19:472–481.
3. Jarnagin WR, Gonen M, Fong Y, et al. Improvement in perioperative outcome after hepaticresection: analysis of 1,803 consecutive cases over the past decade. *Ann Surg*. 2002;236:397–406.
4. Belghiti J, Hiramatsu K, Benoist S, et al. Seven hundred forty-seven hepatectomies in the 1990s: anupdate to evaluate the actual risk of liver resection. *J Am Coll Surg*. 2000;191:38–46.
5. Capussotti L, Ferrero A, Vigano L, et al. Bile leakage and liver resection: where is the risk? *Arch Surg*. 2006;141:690–694. discussion 695.
6. Cescon M, Vetrone G, Grazi GL. Trends in perioperative outcome after hepatic resection: analysis of 1500 consecutive unselected cases over 20 years. *Ann Surg*. 2009;249:995–1002.
7. Lo CM, Fan ST, Liu CL. Biliary complications after hepatic resection: risk factors, management, and outcome. *Arch Surg*. 1998;133:156–161.
8. Imamura H, Seyama Y, Kokudo N, et al. One thousand fifty-six hepatectomies without mortality in8 years. *Arch Surg*. 2003;138:1198–1206.
9. Zimmitti G, Roses RE, Andreou A, et al. Greater Complexity of liver surgery is not associated with an increased incidence of liver-related complications except for bile leak: an experience with 2,628 consecutive resections. *J Gastrointest Surg*. 2012.
10. Capussotti L, Ferrero A, Viganò L, Sgotto E, Muratore A, Polastri R. Bile leakage and liver resection: where is the risk? *Arch Surg*. 2006;141:690–694.
11. Lam CM, Lo CM, Liu CL, Fan ST. Biliary complications during liver resection. *World J Surg*. 2001;25:1273–1276.
12. Guillaud A, Pery C, Campillo B, Lourdais A, Sulpice L, Boudjema K. Incidence and predictive factors of clinically relevant bile leakage in the modern era of liver resections. *HPB*. 2013;15:224–229.
13. Nagano Y, Togo S, Tanaka K, et al. Risk factors and management of bile leakage after hepatic resection. *World J Surg*. 2003;27.
14. Tanaka S, Hirohashi K, Tanaka H, et al. Incidence and management of bile leakage after hepatic resection for malignant hepatic tumors. *J Am Coll Surg*. 2002;195:484–489.
15. Yamashita Y, Hamatsu T, Rikimaru T, et al. Bile leakage after hepatic resec- tion. *Ann Surg*. 2001;233:45–50.
16. Figueras J, Llado L, Miro M, et al. Application of fibrin glue sealant after hepatec-tomy does not seem justified: results of a randomized study in 300 patients. *Ann Surg*. 2007;245:536–542.
17. Tzeng CW, Fleming JB, Lee JE. Yield of clinical and radiographic surveillance in patients with resected pancreatic adenocarcinoma following multimodal therapy. *HPB*. 2012;14:365–372.
18. Nagino M, Kamiya J, Uesaka K, et al. Complications of hepatectomy for hilar cholangiocarcinoma. *World J Surg*. 2001;25:1277–1283.
19. Ijichi M, Takayama T, Toyoda H, Sano K, Kubota K, Makuuchi M. Randomized trial of the usefulness of a bile leakage test during hepatic resection. *Arch Surg*. 2000;135:1395–1400.
20. Li J, Malagó M, Sotiropoulos GC, et al. Intraoperative application of "white test" to reduce postoperative bile leak after major liver resection: results of a prospective cohort study in 137 patients. *Langenbeck's Arch Surg*. 2009;394: 1019–1024.
21. Liu Z, Jin H, Li Y, Gu Y, Zhai C. Randomized controlled trial of the intraoperative bile leakage test in preventing bile leakage after hepatic resection. *Dig Surg*. 2012;29:510–515.
22. Ochiai T, Ikoma H, Inoue K, et al. Intraoperative real-time cholangiography and C-tube drainage in donor hepatectomy reduce biliary tract complications. *J Gastrointest Surg*. 2011;15:2159–2164.
23. Huang T, Bass JA, Williams RD. The significance of biliary pressure in cholangitis. *Arch Surg*. 1969;98:629–632.
24. Yoshimoto H, Ikeda S, Tanaka M, Matsumoto S. Relationship of biliary pressure to cholangiovenous reflux during endoscopic retrograde balloon catheter cholangiography. *Dig Dis Sci*. 1989;34:16–20.
25. Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien–Dindo classification of surgical complications: five-year experience. *Ann Surg*. 2009;250:187–196.
26. Broering DC, Wilms C, Bok P, et al. Evolution of donor morbidity in living related liver transplantation: a single-center analysis of 165 cases. *Ann Surg*. 2004;240:1013–1024.
27. Shio S, Yazumi S, Ogawa K, et al. Biliary complications in donors for living donor liver transplantation. *Am J Gastroenterol*. 2008;103:1393–1398.
28. El-Meteini M, Hamza A, Abdalaal A, et al. Biliary complications including single- donor mortality: experience of 207 adult-to-adult living donor liver transplantations with right liver grafts. *HPB*. 2010;12:109–114.
29. Taketomi A, Morita K, Toshima T, et al. Living donor hepatectomies with procedures to prevent biliary complications. *J Am Coll Surg*. 2010;211:456–464.
30. Shin M, Song S, Kim JM, et al. Donor morbidity including biliary complications in living-donor liver transplantation: single-center analysis of 827 cases. *Transplantation*. 2012;93:942–948.
31. Sultan AM, Salah T, Elshobary MM, et al. Biliary complications in living donor right hepatectomy are affected by the method of bile duct division. *Liver Transplant*. 2014;20:1393–1401.
32. Dirican A, Ara C, Kutluturk K, et al. Donor postoperative biliary complications after living-donor liver transplant. *Exp Clin Transpl*. 2015;30:516–523.
33. Leelawat K, Chaiyabutr K, Subwongcharoen S, Treepongkaruna SA. Evaluation of the white test for the intraoperative detection of bile leakage. *HPB Surg*. 2012;2012:425435.
34. Ijichi M, Takayama T, Toyoda H, et al. Randomized trial of the usefulness of a bile leakage test during hepatic resection. *Arch Surg*. 2000;135:1395–1400.
35. Suehiro T, Shimada M, Kishikawa K, et al. In situ dye injection bile leakage test of the graft inliving donor liver transplantation. *Transplantation*. 2005;80: 1398–1401.
36. Kaibori M, Ishizaki M, Matsui K, Kwon AH. Intraoperative indocyanine green fluorescent imaging for prevention of bile leakage after hepatic resection. *Surgery*. 2011;150:91–98.
37. Sakaguchi T, Suzuki A, Unno N, et al. Bile leak test by indocyanine green fluorescence images after hepatectomy. *Am J Surg*. 2010;200:e19–e23.