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Cross-sectional Study

The use of Thulium-Doped Fiber Laser (TDFL) 1940 nm as an energy device in liver parenchyma resection, a-pilot-study in Indonesia

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A R T I C L E I N F O

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Liver surgery
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A B S T R A C T

Introduction: Several modalities are used to improve the outcome of liver resection surgery. Laser-based surgery may become promising option; therefore we aim to report our experience regarding the efficacy and safety of Thulium-Doped Fiber Laser (TDFL) 1940 nm in liver parenchyma resection.

Methods: A cross sectional study in which patients with pre-existing liver pathology during July 2019 and July 2020 were randomly assigned to receive liver resection using TDFL integrated with raman laser emitting at 1940 nm and 1470 nm wavelength. Data on estimated blood loss during liver transection, liver transection speed, morbidity rate, and postoperative variables including complications, length of hospital stay (days), and mortality were analyzed.

Results: A total of 17 consecutive liver resections were performed, among them are 7 major and 11 minor hepatectomies. The Multipulse TM+1470 were used on 8 procedures consisted of 1 major and 7 minor hepatectomies, the mean amount of blood loss during operation and liver transection was 628.13 $\pm$ 141.31 mL and 294.63 $\pm$ 94.81 ml, respectively. The mean liver transection speed was 1.52 $\pm$ 0.27 cm^2/min. No biliary leak, post-hepatectomy-liver failure, and mortality were reported.

Conclusion: TDFL provided by Multipulse TM+1470 is an effective and safe tool for liver surgery, providing good hemostasis and allowing for safe and effective exposure of vascular. Further study with larger samples might be needed proved the efficacy and safety of TDFL in liver surgery.

1. Introduction

Liver resection is a complex and evolving procedure [1]. The role of liver surgery is increasing with proven advantages in the primary and secondary liver tumor. Blood loss is one of the important factor in determining the mortality and morbidity of liver resection [2–4]. The liver parenchyma resection or transection is a challenging step of liver surgery and have high bleeding risk.

Different kinds of energy devices were invented in order to minimize bleeding from the transection of the liver parenchyma. Several modalities in liver parenchyma resection include the crush clamp technique, ultrasonic dissector (harmonic scalpel and Cavitron Ultrasonic Surgical Aspirator/CUSA), and an advanced technique like bipolar as sealing devices (Ligasure Vessel sealing system), water jet dissector, and surgical stapler. Modern techniques such as Ligasure and harmonic scalpel are associated with less bleeding, shorter transection time, and fewer vessels ligation compared to crush clamp technique, however they were associated with higher risk of post-operative bile leak complication [5–8].

Laser based surgery has been utilized in many different medical fields. The CO_2 laser is used to vaporize tissue and the Neodymium: Yttrium–Aluminum-Garnet (Nd:YAG) laser that caused coagulative necrosis tissue [9]. The laser effect on tissue is dependent on both properties of the tissue as well as the laser [10]. The main biological targets that are dealt with, absorb light in variable quantity, and their optimum absorption spectrum depend on the wavelength of the incident photon energy. The newest energy device for resection of solid organ parenchyma is Thulium laser. In the author's hospital, the available laser-based surgery is a Thulium-doped fiber laser (TDFL) emitting at 1940 nm integrated with 1470 nm Raman laser combined in the same desired fiber optic (Jenna surgery Multipulse Tm+1470). The use of TDFL in solid organ parenchyma surgery is still uncommon. Boguslawa et al., showed the zones of thermal tissues achieved by TDFL were narrower compared to Diode Laser and Nd:YAG laser, therefore TDFL laser seems to be an

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effective tool for precise surgical procedures with narrow and controlled zone of destruction of the adjacent tissue [11]. Maciej et al., showed the efficacy of TDFL in cutting with a narrow zone of thermal injury and provides good hemostasis during partial liver resection and liver tissue incision. TDFL operating at 1940 nm may be a potential tool in oncologic liver surgery, especially when healthy tissue sparing is a priority and small atypical excisions are performed [12].

In this pilot study, we report the efficacy and safety in liver parenchyma transection using the TDFL emitting at 1940 nm integrated with a 1470 nm Raman laser as an energy device to aid the cutting and coagulation of liver parenchyma (Fig. 1).

2. Methods

2.1. Terminology

The terminology for liver anatomy and resections is based on Brisbane classification [13]. Hepatic resections are considered major if at least 3 adjacent segments are removed. Post hepatectomy liver failure (PHLF) determined using International Study Group of Liver Surgery (ISGLS) criteria, which are characterized by an increased International Normalized Ratio (INR) and concomitant hyperbilirubinemia on or after postoperative day 5 [14]. Postoperative mortality was defined as any death resulting from a complication during surgery analyzed in 90-days period.

2.2. Patients and study design

This pilot study is a cross-sectional study in which adult patients aged more than 18 years old with pre-existing liver pathology from a single academic hospital (Prof dr. R.D. Kandou General Hospital, North Sulawesi) were randomly assigned to receive liver resection using TDFL integrated with raman laser emitting at 1940 nm and 1470 nm wavelength (Jenna surgery Multipulse Tm+1470). Informed consent was obtained after full explanation of the surgery plan and the goal of this study. Patients who refused to be operated or deemed unfit by the surgery or anesthesia team will be excluded. Estimated blood loss during liver transection was used as the primary end point, whereas liver transection speed and morbidity rate were used as the secondary end points. Intraoperative data, including operative time (minutes), liver transection time (minutes), liver transection area (cm^2), portal triad clamp time (Pringle time; minutes), estimated blood loss during liver transection and operation (ml) were recorded for subsequent analysis. All patients were assessed for postoperative variables including complications, length of hospital stay (days), and mortality. Postoperative complications are assessed during hospitalization and one week after discharge in our surgical outpatient department. Assessment of 90-days-mortality were made by calling the patients or the patient family. This study is exempt from ethical approval in our institution. This study has been registered in www.researchregistry.com with registration unique identifying number (UIN): researchregistry6231 (https://www.researchregistry.com/browse-the registry#home/registrationdetails/5fa751ab769cd40015b743c8/). This result of study will be reported in line with the STROCSS criteria [15].

2.3. Surgical technique

A single liver surgeon (M.T.) performed all of the liver resections. Liver transection was performed using a TDFL integrated with raman laser (Multipulse TM+1470) and an "on demand" pringle maneuver with 15-min periods of clamping and 5-min periods of unclamping were performed if necessary. The power of the Multipulse TM+1470 was set at the 110-W for the TDFL with the duration of 50.0 ms and the speed of 4 Hz, accompanied with the coagulation function of the raman laser set at the power of 15-W, duration of 25.0 ms, and the speed of 4 Hz. The Glissonean sheaths pedicle and the main hepatic veins were ligated, whereas the small veins branch were clipped. Extrafascial Glissonean pedicle approach were used for liver hilar control in all Multipulse TM+1470 group.

3. Results

Between July 2019 and July 2020, a total of 17 consecutive liver

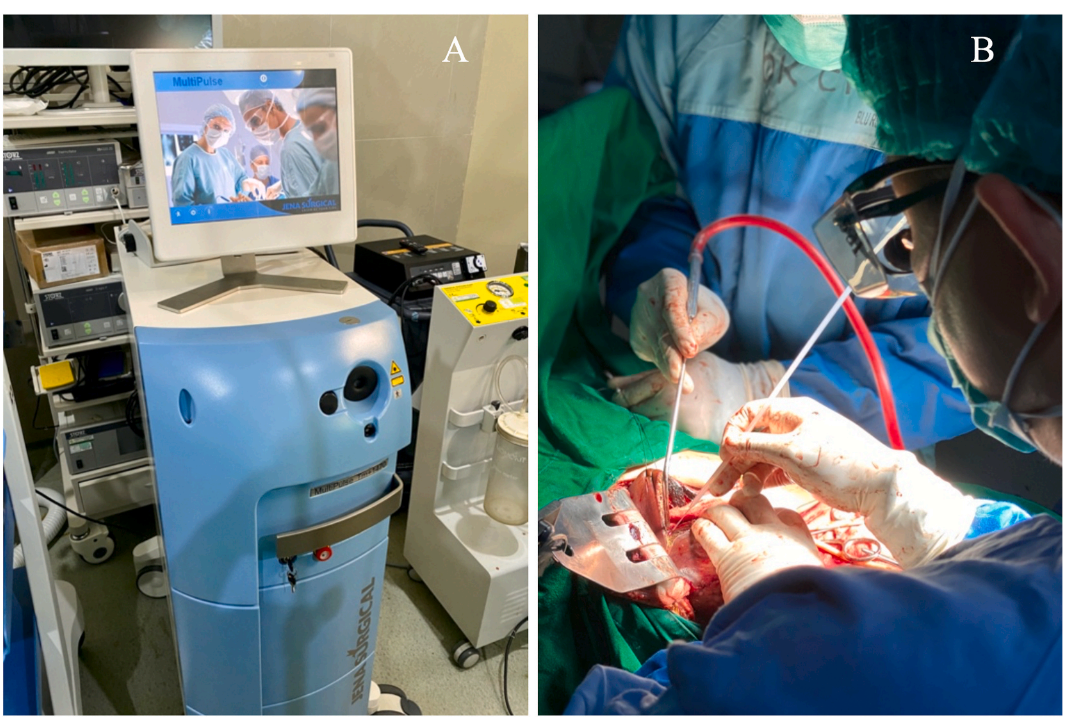

Fig. 1. A. The Multipulse TM +1470 nm emitting the Thulium laser at 1940 nm and Raman laser at 1470 nm, **B.** The TDFL being used by the author as an energy device to perform liver parenchyma resection.

resections were performed, among them are 7 major and 11 minor hepatectomies, with the postoperative mortality rate of 23.5%. The Multipulse TM+1470 were used as an energy device on 8 procedures consisted of 1 major and 7 minor hepatectomies (Table 1). Among 17 patients, five patients were diagnosed with synchronous metastases arising from gastrointestinal malignancy, and four of them were in the Multipulse TM+1470 group. Out of these 4 patients, liver resections were performed synchronously after resection of the primary tumor in 2 patients, staged liver metastasis resection was performed in 1 patient, and "liver first" strategy was performed in another 1 patient. One patient in each Multipulse TM+1470 group and other energy devices group required right hepatic vein resection because of metastatic invasion from a primary colorectal cancer and a gastric GIST, so Systematic Extended Right Posterior Sectionectomy (SERPS) were performed (Fig. 2) [16].

For all patients in Multipulse TM+1470 group (Table 2), the mean ± standard deviation amount of blood loss during operation and liver transection was 628.13 ± 141.31 ml and 294.63 ± 94.81 ml, respectively. The mean liver transection speed was 1.52 ± 0.27 cm^2/min. The Pringle maneuver was performed in 4 out of 8 patients, with the mean time of 8.75 ± 3.87 min. The morbidity and mortality rate in the Multipulse TM+1470 group were 25% and 0%, respectively. The postoperative complications are listed in Table 3 and occurred in 2 patients (25%) in the manifestation of ascites, but no major complications requiring surgical intervention were encountered. The mean duration of postoperative hospital stay was 8.5 ± 0.96 days. Due to the severity of the procedure, in 2 patients whom synchronous liver resection and resection of colorectal malignancy were performed, the postoperative hospitalization reached up to 14 and 10 days.

The PHLF were not detected in all 8 procedures using the criteria made by ISGLS, the complete database of the postoperative level of total bilirubin serum and INR is shown in Table 4.

Table 1
Patients characteristics.

Characteristics	Total (n = 17)	Multipulse TM + 1470 (TDFL) (n = 8)
Age mean ± standard deviation, years old	56.5 (2.23)	57.38 (3.74)
Male, n (%)	11 (64.71)	6 (75)
Cause of disease, n (%)		
Metastatic liver tumor	5 (29.4)	4 (50)
Hepatocellular carcinoma	7 (41.2)	2 (25)
Cholangiocarcinoma	2 (11.8)	0 (0)
Other benign etiology or Polycystic liver disease	3 (17.7)	2 (25)
Background liver (n)		
Normal	14 (82.4)	8 (100)
Cirrhosis or chronic hepatitis	3 (17.7)	0 (0)
Tumor		
Size (cm)		
<5	1 (0.06)	0 (0)
≥5	16 (94.1)	8 (100)
Number		
Single	12 (70.6)	7 (87.5)
Multiple	5 (29.4)	1 (12.5)
Type of hepatectomy, n (%)		
Major		
Extended hemihepatectomy	3 (17.7)	0 (0)
Hemihepatectomy	4 (23.5)	1 (12.5)
Minor		
Segmentectomy	8 (47.1)	5 (62.5)
Limited resection	2 (11.8)	2 (25)
Number of resections, n (%)		
Single	12 (70.6)	7 (87.5)
Multiple	5 (29.4)	1 (12.5)
Combined Resection and Reconstruction, n (%)		
Colorectal resection	2 (11.8)	2 (25)
Hepatic vein resection	2 (11.8)	1 (12.5)

4. Discussion

Liver resection remains a surgery with a chance of complications, where blood loss is the most serious concern. Blood loss may related with mortality and morbidity of liver resection [[2–4]]. Various vascular occlusion techniques and different techniques-devices are utilized to minimize bleeding. This study presented the use of TDFL as part of laser-based surgery, as an energy device in liver parenchyma transection with the blood loss as a primary end point. Other parameters evaluated are liver transection speed and postoperative morbidity and mortality.

In the mid 1980s, different lasers types were tested for their feasibility in liver surgery. Nd:YAG laser was compared with ultrasonic surgical aspirator and blunt dissection in a dog model for liver resection but was not superior to the other two techniques in particular due to a larger zone of thermal damage, while CO_2 laser had a better cutting efficiency and produced a narrower thermal damage zone approximately 1.5 mm wide, but it did not provide hemostasis [17,18]. Hence, both types of lasers were not superior to non-laser techniques for liver parenchyma transection, and thus the laser technique had not been transposed to a clinical practice. TDFL was invented with expectations to achieve excellent hemostasis and a narrower thermal damage zone.

TDFL in this study come in the form of Multipulse TM+1470 and is a promising device in liver surgery due to some favorable features. First, TDFL operates at a wavelength of 1940 nm, which corresponds to the wave length of light that is highly absorbed by water, most of the soft tissues including the liver is characterized by an abundance of water, thus results in a shallow penetration of laser energy into the tissue, and followed by a strong local thermal effect that did not damage the deeper structures, makes a greater precision of the procedure. Maciej et al. states that TDFL had a very good cutting properties while the total depth of thermal changes in the liver tissue ranges from 0.62 to 1.82 mm depending on the time of evaluation. Similar width of the thermal damage zone (less than 2.0 mm) was reported in an experimental pig model for partial nephrectomy with TDFL [12,19,20]. TDFL also has potent local thermal effect resulting in its ability to cut and coagulate, thus providing hemostasis. Hemostasis property of the laser is important in surgery of highly vascularized tissues such as the kidney, spleen, or liver. The use of CO_2 laser in liver resection may provide efficient cutting without hemostasis [18]. Our study showed that TDFL may provide a good bleeding control during hepatic transection reflected by the low mean estimated blood loss during parenchyma transection (294.63 ± 94.81 ml). Studies have reported that blood loss in patients undergoing liver resection in patients in specialized hospital centers ranged from 500 to 2400 mL [21–23]. While other studies using different energy devices such as Ligasure recorded that the blood loss during transection is at 200 ml, and with the use of harmonic scalpel the blood loss is at 516.67 ml [5,6]. Another study by Bodzin et al., using CUSA as the energy device in parenchymal liver transection showed a median estimated blood loss of 1035 ml, ranging from 0 to 5850 ml [24].

The liver parenchyma transection is comprised of 2 separate procedures. The first step is crushing the liver parenchyma and subsequent aspiration of the crushed tissue and blood to expose the intrahepatic vessels, which is commonly achieved by the use of CUSA. The second step is ligation or sealing of the exposed vessels, which is typically achieved by manual ligation, clips, or electric cautery. The laser beam emitted by TDFL in our opinion could perform the first step well, but from our experience, it is unable to seal exposed vessels and biliary tracts, so manual ligation and the use of surgical clips are applied. This condition might explained the liver transection speed in our study at 1.52 ± 0.27 cm^2/min, which is slightly slower compared with transection speed using conventional crush clamping technique and manual vessels ligation at 1.6 cm^2/min, but more than half the speed of Ligasure which was at 2.3 cm^2/min as an energy device in liver transection [5]. In our study, out of 8 patients with TDFL use, seven patients were categorized as minor hepatectomies, non-anatomic resection and

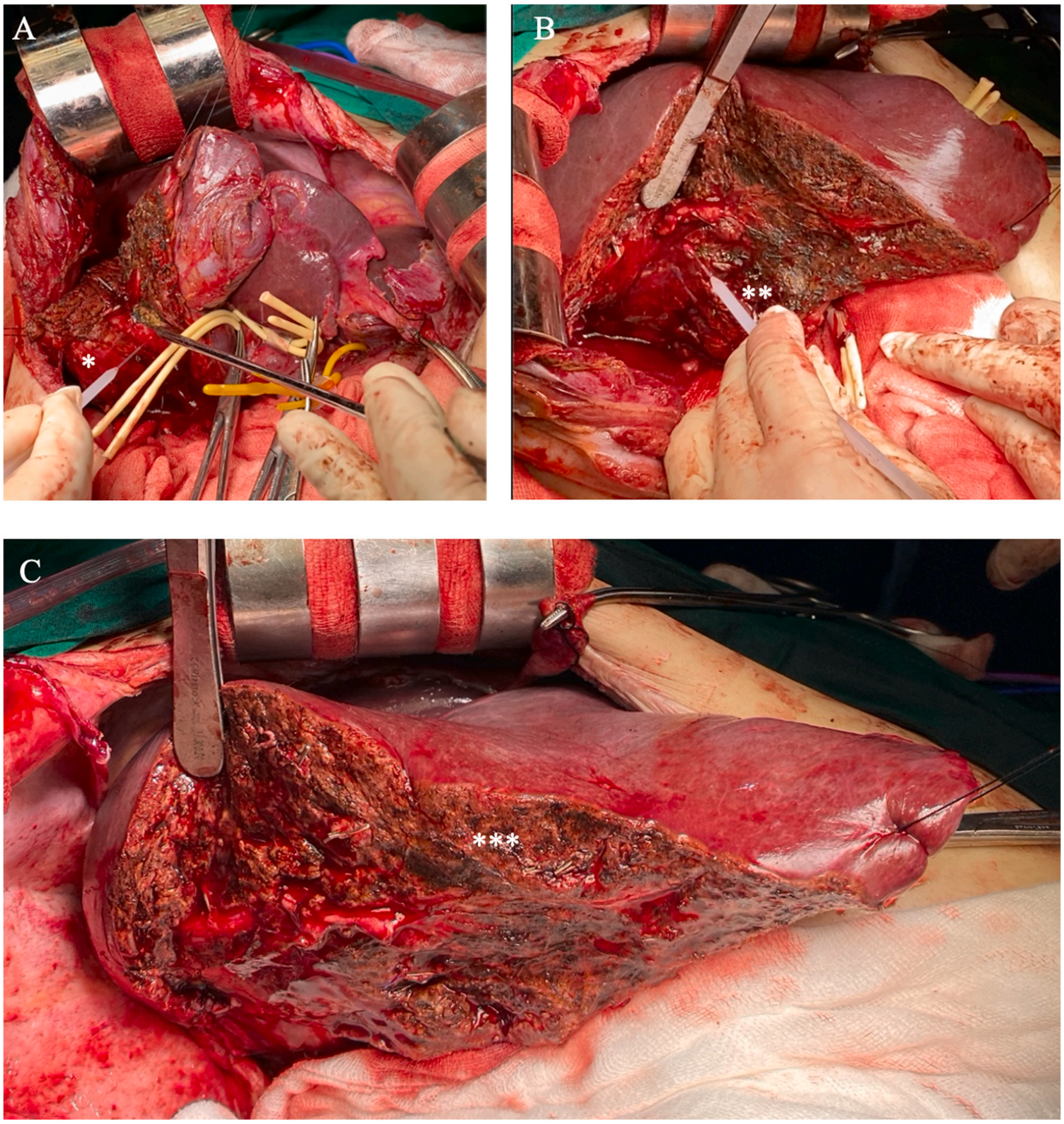

Fig. 2. A. The TDFL cutting function in Systematic Extended Right Posterior Sectionectomy (SERPS), the minuscule tip of laser fiber **(*)** able to cut the parenchyma with close proximity to major vascular and biliary structures, **B.** The coagulation function **(**)** for hemostasis from the raw liver surface, **C.** The liver parenchyma transected plane **(***)** by TDFL showed excellent hemostasis and no bile leakage.

Table 2
Surgical outcomes in liver parenchyma transection using Multipulse TM+1470 (TDFL).

Outcomes	Multipulse TM + 1470 (TDFL) (n = 8)
Blood loss (ml)	
Total	628.13 ± 141.31
During transection	294.63 ± 94.81
Liver transection	
Time (min)	66.13 ± 11.66
Area (cm^2)	106.57 ± 27.70
Speed (cm^2/min)	1.52 ± 0.27
Pringle maneuver time (minutes)	8.75 ± 3.87
Perioperative blood transfusion (units)	1.13 ± 0.35

All values are expressed as mean ± standard deviation.

Table 3
Surgical complications in liver parenchyma transection using Multipulse TM+1470 (TDFL).

Complications	Multipulse TM + 1470 (TDFL) (n = 8)
Postoperative hospital stays (day)	8.5 ± 0.96
Mortality, n (%)	0 (0)
Morbidity, n (%)	2 (25)
Bile leak	0 (0)
Ascites or pleural effusion	2 (25)
Ileus	0 (0)
Catheter infection	0 (0)
Lung edema	0 (0)
Adrenal hemorrhage	0 (0)

hemihepatectomy procedures differed in terms of control of inflow blood and the shape of the transection plane. This is important because less inflow blood control may result in increased blood loss from the transection plane because the vessel stumps of the resected side are left-open in the ordinary manual ligation method. The transection surface is generally flat and simple during major hepatectomy but is often concave and complex during minor hepatectomy. These conditions explained the slower transection speed in our study. On the other hand, considering the majority of complex transection planes in this study and the mean blood loss during transection of 294.63 ± 94.81 ml, the use of TDFL as an energy device provides good hemostasis and coagulation function.

Table 4
Post Hepatectomy Liver Failure criteria based on the increase of total bilirubin and INR on postoperative day 5 in Multipulse TM+1470 (TDFL) group.

No	Patient	Age	Diagnosis	Type of resection	Total bilirubin (mg/dl)/ INR postoperative day 1	Total bilirubin (mg/dl)/ INR postoperative day 3	Total bilirubin (mg/dl)/ INR postoperative day 5	PHLF by ISGLS
1	♂	66	HCC segment 6	Anatomical segmentectomy 6	1.18/1.40	2.60/1.39	1.30/1.32	None
2	♂	61	MCRC segment 7-8	Non-anatomical metastasectomy segment 7-8	1.41/1.35	0.70/2.29	0.84/1.40	None
3	♂	51	GIST liver metastasis segment 6-7	SERPS (Segment 6–7 + RHV)	0.88/3.19	0.68/1.99	0.56/1.54	None
4	♂	70	MCRC segment 3,7	Non-anatomical metastasectomy segment 3,7	0.28/1.29	0.78/1.49	0.45/0.95	None
5	♀	66	HCC segment 5-6	Non-anatomical liver resection Segmentectomy 5-6	1.02/1.33	1.39/1.30	0.93/1.25	None
6	♂	55	HCC segment 5	Anatomical segmentectomy 5	3.66/1.47	2.45/1.41	1.54/1.34	None
7	♂	44	MCRC segment 7-8	Bisegmentectomy 7-8	1.26/1.46	1.29/1.27	0.62/1.34	None
8	♀	46	Policystic liver disease	Right Hepatectomy	0.89/1.63	1.06/1.24	0.64/1.07	None

*HCC = Hepatocellular Carcinoma, MCRC = Metastase Colorectal Cancer, GIST = Gastro Instestinal Stromal Tumor, SERPS = Systematic Extended Right Posterior Sectionectomy, PHLF = Post Hepatectomy Liver Failure.

The present study also demonstrates the morbidity and mortality of liver resection procedure. Morbidities are related to bile leak, which is one of the most common complications after liver resection with the incidence rate between 6.5% and 27.2% [25–30]. After resections with biliary reconstruction using biliodigestive anastomoses (BDA), leak rates increase to 36.9% [31], while rates are lower when the extrahepatic bile duct preserved (3.6–8.0%) [32–37]. Bile leaks occurred significantly more often in patients with diseases of the biliary tract compares to patients with other indications (23.6% vs. 11.3%). The bile leak incidence also occurred more common in major liver resections and BDA reconstruction [38]. In this TDFL study, no bile leaks were observed. The absence of bile leak incidence might be due to the ability of TDFL in exposing the biliary and vascular structures of the liver parenchyma, hence enabling it to be sealed using clips or manual ligation later on, although from our experience, TDFL itself is unable to seal major bile ducts.

The PHLF incidence reported ranging from 0.7 to 35% [38] It varies according the underlying pre-operative status of the liver and the underlying pathology requiring liver resection [39–41]. The incidence of PHLF in our study was valued using the parameters set by ISGLS, and no PHLF were found, despite most of the underlying diseases are hepatocellular carcinoma and colorectal liver metastasis. These might be due because most of the procedure performed were minor hepatectomies leaving most of the healthy liver parenchyma, which can be seen in bilirubin and INR levels from post-operative day 1, 3, and 5.

The minuscule glass fiber of the TDFL provided by Multipulse TM+1470 might have its own advantages and disadvantages. The minuscule size advantages are its applicable for cutting and coagulating of the liver parenchyma in small and narrow crevices close to major and/or important vascular and biliary structures. On the other hand, the disadvantage is the gripping sensation while using the TDFL, due to its small handle making it harder to hold and maneuver. In order to overcome this problem, the author usually use an endo-loop sleeve commonly applied in laparoscopic procedure, where the laser fiber is inserted inside the endo-loop sleeve making it easier to hold. The mean postoperative hospital stay in our study was 8.5 ± 0.96 days, shorter than other studies being reported using Ligasure (11 days) and conventional technique (13.5 days) [5]. The laser fibers are re-useable and can be sterilized, based on the shortened use of the operating room and length of hospital stay, use of the TDFL is highly cost-effective.

The strength of our study is the novelty of TDFL usage in liver resection, which may serve reference for further studies and add evidence regarding the use of laser device in liver surgery. The limitation of our study is the small number of subjects, being only performed in single institution, and no direct comparison of effectiveness or safety between TDFL and other modalities were made.

5. Conclusion

TDFL provided by Multipulse TM+1470 is an effective and safe tool for liver surgery. Providing good hemostasis and also allows for safe and effective exposure of vascular and biliary structures without increasing the rate of bile leak and PHLF incidence. Further study with more samples might be needed to test the efficacy and safety of TDFL in liver surgery.

Declaration of competing interest

The authors declare that there is no conflict of interest.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2020.11.039.

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Ethical approval

This study is exempt from ethical approval in our institution.

Author contribution

Michael Tendean: Study concept and design, perform the surgery protocol, data collection, data analysis, writing the paper.

Toar D.B Mambu: Study concept and design, data collection, data analysis, writing the paper.

Ferdinand Tjandra: Study concept and design, data collection, data analysis, writing the paper.

Jimmy Panelewen: Study concept and design, data collection, data analysis, writing the paper.

Trial registry number

1. Name of the registry: researchregistry.com.
2. Unique Identifying number or registration ID: researchregistry6231.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse-the%20registry#home/registrationdetails/5fa751ab769cd40015b743c8/

Guarantor

Michael Tendean.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

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