Cut surface biliary complications in open and laparoscopic liver resections

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Abstract

Background/Aims

Aim of our study was to analyze surgical parameters and postoperative morbidity with special emphasis on cut surface biliary leakage (BL), after launching a minimally invasive liver resection program at our center.

Patients and methods

A prospectively maintained medical database of patients who required liver resection was used for analysis. Exclusion criteria were liver resections with biliodigestive anastomosis. Clinicopathological characteristics and outcomes were analyzed retrospectively.

Results

A total of 141 patients were divided into a group of 47 patients (33.3%) receiving laparoscopic (LLR) and 94 patients (66.7%) undergoing open liver resections (OLR). We performed 62 major OLR (66.0%) and 31 major LLR (66.0%). In comparison with the LLR group, operation time was longer (326 ± 97 minutes vs. 287 ± 133 minutes; P = 0.080) and average blood loss was higher in the OLR group (529 ± 441 mL vs. 356 ± 459 mL; P = 0.052), without showing significancy. In the LLR group, morbidity was significantly lower than in the OLR group (OLR vs. LLR: 19 (20.2 %) vs. 3 (6.4%); P = 0.033). Overall BL rate was 4.3% (N = 6). All BL occurred in patients after OLR and were associated with a significantly longer hospital stay (hospital stay with biliary leakage vs. hospital stay without biliary leakage: 37.3 ± 19.3 days vs. 14.7 ± 11.1 days; P < 0.001).

Conclusion

The introduction of different transection techniques in laparoscopic liver resections did not increase morbidity and BL rate.

Introduction

Modern surgical treatment of the liver includes the use of minimally invasive resection techniques for benign and malignant disease (1). The initial experience with laparoscopic liver surgery demonstrated that even major resections could be performed with acceptable morbidity and mortality, in a selected group of patients and in specialized centers. A multimodal therapeutical approach introducing state-of-the-art intraoperative visualization techniques (2, 3) and advanced resection strategies (4) may furthermore increase the feasibility and safety of laparoscopic liver resections. However, because of a steep learning curve, a formal structure of minimally invasive liver surgery training and application might be of particular importance for surgeons working in specialized liver tumor centers.

Biliary leakage (BL) remains the Achilles heel of liver surgery and accounts for a major fraction of postoperative complications (5), and may require interventional procedures or even re-laparotomy in certain cases (6). Although laparoscopic liver surgery has demonstrated several advantages when compared to open liver surgery a recent meta-analysis revealed a higher bile leakage rate for laparoscopic left hemi-hepatectomies in patients with hepatolithiasis (OR, 1.7; P = 0.01) (9). Although no causal explanation for this phenomenon could be provided, one possible reason might be differences in the technique of parenchymal transection and bile duct closure during implementation of laparoscopic liver surgery. Like in other minimally invasive procedures, many surgeons are using either advanced bipolar or ultrasonic shears or linear cutters for parenchymal transection rather than an ultrasonic dissector as mainly used in open surgery (10). It remains unclear, if the change of the parenchymal transection with e.g. use of ultrasonic shears might be afflicted with a higher rate of bile leaks or if this might only be the case when used in inflamed or cholestatic liver parenchyma (9).

In view of the formation of a specialized high-volume liver tumor center, we recently introduced minimally invasive liver resections into the portfolio of our surgical treatment modalities. The aim of our study was to analyze our patient data regarding surgical outcome and post-operative morbidity. Special emphasis was given to biliary leak occurrence after open (CUSA based) and laparoscopic (ultrasonic shears based) liver resections.

Patients And Methods

Study design and patient demographics

The study was approved by the ethics committee of the University of Leipzig, number 142/18-EK and the study protocol was performed in accordance with the relevant guidelines. Informed consent was waived by the ethics committee of the University of Leipzig due to the retrospective nature of the study.

The medical data of patients who received liver resections at our department between April 2016 and September 2017 was reviewed retrospectively. Patients receiving a biliodigestive anastomosis were excluded. Data were collected from anesthesiologic and operative documentation of the patient’s history, the intraoperative procedure, histological results, the process at the intensive care unit and the medical discharge report. The Patients were split according to the surgical technique into laparoscopic liver resections (LLR) and open liver resections (OLR). OLRs were graded according to the Brisbane 2000 terminology of liver anatomy and resections (11) and LLRs were graded according to the difficulty scoring system described by Di Fabio et al (12). Medical data analysis comprised patient demographics (age, sex, body mass index), pre-operative performance status according to ASA (American society of Anesthesiology) class I to III, and intraoperative surgical data (operation time, blood loss, transfusion requirement (defined as units of red cell concentrate, albumin or fresh frozen plasma substitution), pringle maneuver, bile duct drain and T-drain placement, intrabdominal drain placement, extent of resection, lymphadenectomy), histopathologic findings and post-operative data (length of hospital stay, postoperative complications during the hospital stay).

Primary endpoint of the study was the evaluation of biliary leakage (BL) after liver resection. BL was detected via macroscopic and serologic detection of bile in the abdominal drainages. Furthermore, patients suspicious for bile leakage (increase infection parameters, fever, tachycardia) and with radiological signs (determined by ultrasound (US) or computed tomography (CT)) of intrabdominal fluid collections after surgery underwent US or CT guided needle puncture and drain placement. Biliary leakages were graded according to Koch et al. (6). BL is defined as fluid with an elevated bilirubin level in the abdominal drain or intrabdominal fluid and can be graded as A, B or C depending on the required treatment method. This can comprise (A) no or little change in the patient's clinical management, (B) a change in the clinical management (e.g. additional diagnostics and interventional procedures) without the need for re-laparotomy and (C) a bile leakage requiring re-laparotomy (6). Secondary endpoints were short-term complications and short-term survival.

Surgical technique of open liver resection (OLR)

Open liver resections were performed as described earlier by our group (13) (14). Vascular inflow and outflow control before parenchymal transection remain the mainstay of our technique for anatomic resections. For the vascular inflow control a tourniquet was placed around the hepatoduodenal ligament and closed on demand. Parenchymal transection was performed with the Caviton Ultrasonic Surgical Aspirator (CUSA). Whereas smaller vascular and biliary structures were divided between titanium clips, larger structures were ligated or suture-ligated. Additional hemostasis was performed by bipolar forceps and irrigation. No hemostatic agents or other sealants of the transection surface was used. A White-Test for intraoperative bile leak testing was performed in all open liver resections. It was performed either via the T-tube or otherwise a cannula was inserted into the cystic duct after cholecystectomy, and a fatty emulsion (5% fat content parenteral nutrition supplement) was injected with gentle pressure. In case of a biliary leakage extravasation of fatty emulsion at the resection surface or structures of the biliary tree a PDS 5 – 0 suture was placed accordingly to close the leakage (15). In case of long exposure of central biliary structures, suture of central biliary ducts, hints for an increased biliary pressure or continued leakage during the 'white test' a T-tube was inserted for biliary decompression. Abdominal drains were avoided as far as possible, especially in patients with liver cirrhosis. However, in patients with extended lymphadenectomy in the retro- / peripancreatic area or in patients with persistent oozing form the transection surface abdominal drains were routinely used.

Surgical technique of laparoscopic liver resection (LLR)

For laparoscopic resections a supine split-leg patient position ('French position') was applied, and the operation table was moved into the Trendelenburg or reverse Trendelenburg position, depending on the operative steps performed. The surgeon was standing between the legs and the assistant was placed to the left side of the patient.

For the vascular inflow control a tourniquet was placed around the hepatoduodenal ligament before parenchymal resection to facilitate an external Pringle maneuver. For right/ extended right hemi-hepatectomies a laparoscopic liver hanging maneuver was considered to reduce bleeding during parenchymal transection (4).

During LLR ultrasonic shears (Harmonic ACE, Ethicon®) were used as mainstay of tissue dissection and parenchymal transection. Coagulation of the cut-surface was performed using bipolar forceps with irrigation, if needed. Smaller biliary and vascular structures were divided with the ultrasonic scissors, medium and larger structures using titanium or absorbable clips.

A laparoscopic CUSA was only used during right or extended right hemi-hepatectomies for exposure of the middle hepatic vein and its tributaries and for intrahepatic exposure of the right bile duct. The other parenchymal division was performed by ultrasonic shears.

Intraoperative ultrasound was used to visualize the tumor and the vascular anatomy in every OLR and LLR procedure. If appropriate, indocyanine green (ICG) fluorescence staining was used for anatomic liver resections to visualize the vascular and biliary anatomy of the liver (2). For direct or indirect tumor staining of e.g. HCC, CCA and CRLM, ICG was applied at different timepoints before surgery (3). Due to inapplicability, a white test was not performed in laparoscopic resections. Also, T-tube were not used during LLR during the study time.

All patients with liver resections received at least overnight intensive care and were transferred to the normal ward earliest the day after surgery.

Statistical analysis

SPSS software, version 25 (SPSS Inc., Chicago, Illinois, USA) and Graphpad Prism software, version 9.2.0 (Graph-Pad Software Inc., La Jolla, CA) were used for statistical analysis and graphs. Welch's t-test for independent samples was used for metric data, so differences in the variability of means could be ignored. Only metric data with sample sizes (n1, n2) smaller than 25 was interpreted with the Wilcoxon-Mann-Whitney-test. Categorial characteristics were evaluated with the Chi-quadrat-test (χ^2-Test), if the sample was higher than 40 in total and if less than 20% of the expected rates where smaller than five. Otherwise the Fisher's exact test was used. A P-value of < 0.05 was accepted as significant.

Results

Patient demographics and indication of liver resection

In the indicated timespan, a total of 141 patients underwent liver surgery in our department. Seven patients received repeat resections within the relevant timespan between both interventions and hence each resection was analyzed and counted individually. The groups were similar in most of their baseline characteristics **Table 1**. In short, 47 (33.3%) liver resections were performed by laparoscopic surgery (LLR) when compared to open liver resections (OLR) in 94 cases (66.7%). The preoperative ASA performance status was significantly worse in patients receiving OLR compared with patients receiving LLR (ASA III: 49 (52.1%) vs. 14 (29.8%)).

A detailed description of the distribution of LLR and OLR regarding diagnosis is given in Fig. 1. Regarding the extent of liver resections, both groups contained a higher percentage of major liver resections (OLR: 62 (66.0%), LLR: 31 (66.0%)), without showing significancy (P = 1.000). Six liver resections which started by minimally invasive surgery were completed as OLR (conversion rate: 12.8%). Reasons for the conversion were laparoscopic inaccessibility (N = 4), intrabdominal adhesions (N = 1), and bleeding from the portal vein (N = 1).

Oncologic LLR were predominantly performed in patients with hepatocellular carcinoma (HCC) (N = 14, 29.8%), followed by patients with colorectal liver metastases (CRLM) (N = 7, 14.9%) and a small percentage of patients with cholangiocarcinoma (CCA) (N = 2, 4.3%). LLR accounted for a good amount of liver resections in patients with benign liver lesions. Radical lymphadenectomy was predominantly performed in OLR (43 (54.7%) vs. 2 (4.3%); P < 0.001).

Surgical parameters and outcome

The average operation time was shorter in laparoscopic resections (when compared to OLR (326 ± 97 minutes vs. 287 ± 133 minutes; P = 0.080). Intraoperative blood loss was slightly higher in OLR (529 ± 441 mL vs. 356 ± 459 mL; P = 0.052). Transfusion requirements were generally low (N = 11, 11.8%), and only necessary in OLR (P = 0.016). Intermittent vascular inflow control (Pringle manoeuvre) was used more often in OLR than in LLR (66 (70.2%) vs. 22 (46.8%); P = 0.007). In our cohort, T-tubes were exclusively used in OLR (47 (50.0%) vs. 0; P < 0.001), and mainly used in patients with malign diseases after lymphadenectomy. Factors associated with T-tube-implantation in patients which underwent OLR are shown in **Table 2**.

A detailed statement about postoperative complications according to the Clavien-Dindo (CD) classification is provided in **Table 3**. Overall morbidity defined as a CD scoring of 3b or higher was n = 22 (15.6%). In LLR morbidity was significantly lower than in OLR (OLR vs. LLR: 19 (20.2%) vs. 3 (6.4%); P = 0.033). The length of hospital stay, was almost twice as high for patients with OLR (hospital stay OLR: 15.5 ± 13.0 days vs. hospital stay LLR: 8.6 ± 5.8 days; P < 0.001). Overall, in-hospital mortality rate was 1.4% (N = 2). LLR were performed without mortality (mortality OLR vs. LLR: 2 (2.1%) vs. 0; P = 0.552).

Biliary leakage

The overall biliary leakage (BL) rate was 4.3% (N = 6). All BL were detected in OLR (P = 0.178). Three BL were graded as type B leakage and were treated with drainages, and three BL were graded as type C leakages and required re-laparotomy. BL occurred after three major resections and three minor resections (P = 0.399). **Table 4** shows the influence of different patient and surgical variables on the development of biliary leakage after OLR. Figure 2 demonstrates the incidence of biliary leakages according to the different liver pathologies. Patients with BL suffered from gall bladder carcinoma (N = 2), cholangiocarcinoma (N = 2), hemangioma (N = 1), and colorectal liver metastasis (N = 1), respectively. Postoperative course with biliary leakage was associated with a significantly longer hospital stay (hospital stay with biliary leakage: 37.3 ± 19.3 days vs. hospital stay without biliary leakage: 14.7 ± 11.1 days; P < 0.001).

Discussion

Our data are in line with previous publications showing that laparoscopic liver resections (LLR) results in shorter operation times, reduced intraoperative blood loss, less wound infections, faster recovery, and hence shorter hospital stay (18). Moreover, it demonstrates that the implementation and adaption of laparoscopic liver surgery does not adversely impact morbidity and mortality in a surgical high-volume liver center.

Biliary leakage remains a serious complication after liver resection with an incidence of up to 12% in previous studies (29). Intraperitoneal septic complications resulting from biliary leakages may lead to secondary organ failure and even death (30) (31). Leakages can derive from previously ligated bile ducts at the resection surface of the liver, either based on a separated biliary system or based on an elevated intrabiliary pressure due to downstream stenosis of the biliary system or papillary dysfunction. Risk factors include prolonged operation time, age, preoperative chemotherapy and special types of liver resections such as left hemi-hepatectomy (33). Moreover, leakage from a bilioenteric anastomosis if performed, is another source of BL (32). In our study bile leaks were detected after three major and three minor open liver resections (P = 0.399). An increased incidence for biliary leakages after left hemi-hepatectomies has been recently highlighted in a meta-analysis on laparoscopic liver resections (9). Fortunately, we did not detect any biliary leakages in our series of LLR which included four laparoscopic left hemi-hepatectomies.

The introduction of a minimally invasive liver resection program at our department did not increase the BL-rate, despite modifications in the technique of parenchymal transection. With 4.3%, the rate of type B or C bile leakages is low in our center and comparable with other studies (35). Prevention of bile leaks may include several measures as: (1) omitting of abdominal drains, (2) meticulous anatomy orientated liver surgery, (3) pre- or intraoperative recognition of variants of the biliary system, (4) application of bile leak tests and (5) eventually biliary decompression e.g., by means of T-tubes in case of complex liver surgery. However, the latter is not supported by enough evidence, so far. All these measures were considered in the present series. The lower rate of bile leaks in patients without abdominal drains has been confirmed in other analysis with an OR of 2.04 (36) to 5.6 (37). During the study period the use of abdominal drains was successively reduced, leading to about 55% of patients without abdominal drains. The ‘white test’ was also adopted liberally in OLR, since it could be shown in a meta-analysis, that its use leads to a significant reduction of postoperative BL (OR 0.3; P = 0.002) (15), however it was not used in LLR. Other measures, which did not prove effective in the prevention of BL like routine application of fibrin sealant was not used at all in the present series. However, surveys e.g. from the Netherlands have shown that more than around 25% of surgeons use fibrin sealants on a frequent/routine basis (38), among others to reduce resection surface-related complications like BL. However, the use of fibrin sealants disproved to reduce the incidence of BL in a meta-analysis (39). However, insertion of a T-tube was afflicted with a (slightly) higher incidence of BL in the present series. Since a T-tube was used mainly in complex cases or in case of long central exposure of the bile duct, this phenomenon is supposed to be based on a consecutive selection of a high risk population for BL based on our previous experience (7) rather than an increased rate of bile leaks caused by T-tube insertion itself. However, this hypothesis cannot be finally proven, but no patient developed BL caused by the T-tube itself, e.g., at the site of insertion into the common bile duct.

However, the incidence of BL in our series is comparable with other analyses, e.g., of the National Clinical Database (NCD) of Japan including 14,970 patients with a revealed a BL-rate of 8.0% (40). In this analysis gallbladder cancer and extrahepatic bile duct carcinoma were also unraveled as risk factors for BL, moreover peripheral vascular disease and open wounds were pointed out as further risk factors.

Postoperative biliary leakages were predominantly detected in patients with Cholangiocarcinoma or gallbladder carcinoma. In our cohort, only two patients with intrahepatic CCA were treated by laparoscopic liver resection. All other CCA patients, and especially those with perihilar cholangiocarcinoma received an open liver resection, as described by our group earlier (13). Reports on laparoscopic liver resection for patients with cholangiocarcinoma (CCA) are still scarce. To date, due to oncological superiority, portal vein embolization for preoperative future liver remnant augmentation and "hilar on block resection" remains our treatment strategy for central bile duct carcinomas (14). However, this type of resection which also requires vascular reconstruction of the portal vein, to date was not performed laparoscopically by our group. Furthermore, postoperative hepatic insufficiency and bile leakage after demanding biliary reconstruction, often with several small orifices, contribute to the postoperative complication rate of this complex surgical disease pattern (46).

Increased experience is commonly paralleled by increased confidence to perform more complex resections. Our overall morbidity and mortality rates are satisfying, especially when compared to the overall German average (50). The rate of other complications was low in the present analysis for LLR as well as OLR, including blood loss and blood transfusions, e.g., compared to NSQIP data (41), where transfusions were required in 33% of patients. Also, the overall morbidity was very low after LLR and significantly reduced compared to OLR. Even the morbidity of the OLR group compares well with other reports from other European centers (35) and clinics from North America (42). However, since patient characteristics differed between both groups, a direct comparison of both groups is debatable. Especially the mortality seems to be rather dependent on patient characteristics than on surgical technique. Likewise, in an analysis using data on 7621 hepatectomies form the US- NSQIP-database (42) it has been shown that mortality after liver resection is predominantly seen in elderly patients in combination with major liver resection. The incidence of post hepatectomy liver failure however was comparatively low in our study, probably due to extensive perioperative liver function testing including the LiMAx test for this selected group of patients.

Limitations

Our study has several limitations. A direct comparison of the minimally invasive and open liver resections is invalid since we did not perform a propensity score matching. Patients in the LLR group hence displayed a better ASA performance status.

Conclusion

We were able to safely develop a minimally invasive liver resection program at our institution which so far resulted in an excellent patient outcome. It could be shown that technical modifications of the surgical approach, like introduction of ultrasonic shears for parenchymal transection are safe and especially not afflicted with an increased rate of biliary leakage or bleeding complications.

Declarations

Ethics approval and consent to participate: The study was approved by the ethics committee of the University of Leipzig, number 142/18-EK and the study protocol was performed in accordance with the relevant guidelines. Informed consent was waived by the ethics committee of the University of Leipzig due to the retrospective nature of the study.

Consent for publication: The current study doesn't involve identity revealing human information, consent for publication is hence not required.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Authors contributions:

Substantial contributions to the conception: RS, SR, HG, DS

Design of the work: RS, SR, HG, ES, AL, TB, CH, DS

Acquisition, analysis of data: SR, HG

Interpretation of data: SR, HG, US

Drafted the work or substantively revised it: RS, SR, HG, ES, AL, TB, CH, DS, US

Have approved the submitted version (and any substantially modified version that involves the author's contribution to the study): RS, SR, HG, ES, AL, TB, CH, DS (all authors)

Have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature: RS, SR, HG, ES, AL, TB, CH, DS, US (all authors)

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Tables

Tables 1 to 4 are available in the Supplementary Files section.

Figures

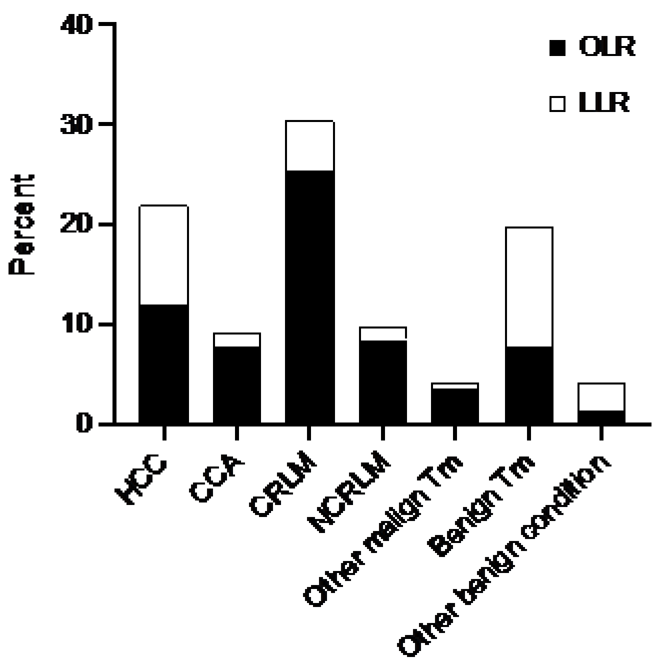

Figure 1

Distribution of LLR and OLR regarding diagnosis. Group of “other malignant tumors” include: gallbladder carcinoma (N = 4, 2.8%), angiosarcomas (N = 1, 0.7%) and leiomyosarcomas (N = 1, 0.7%). Benign liver tumors included patients with adenomas (N = 6, 4.3%), focal nodular hyperplasia (N = 7, 5.0%), angiomyolipoma (N = 1, 0.7%), and hemangioma (N = 7, 5.0%). Group of “other benign conditions” include: Caroli disease (N = 5, 3.5%), echinococcus cyst (N = 2, 1.4%), benign bile duct stenosis (N = 1, 1.4%), hematoma (N = 2, 1.4%), liver abscess (N = 1, 0.7%) and polycystic liver disease (N = 1, 0.7%). CCA, cholangiocarcinoma; CRLM, colorectal liver metastases; HCC, hepatocellular carcinoma; nCRLM, non-colorectal liver metastases.

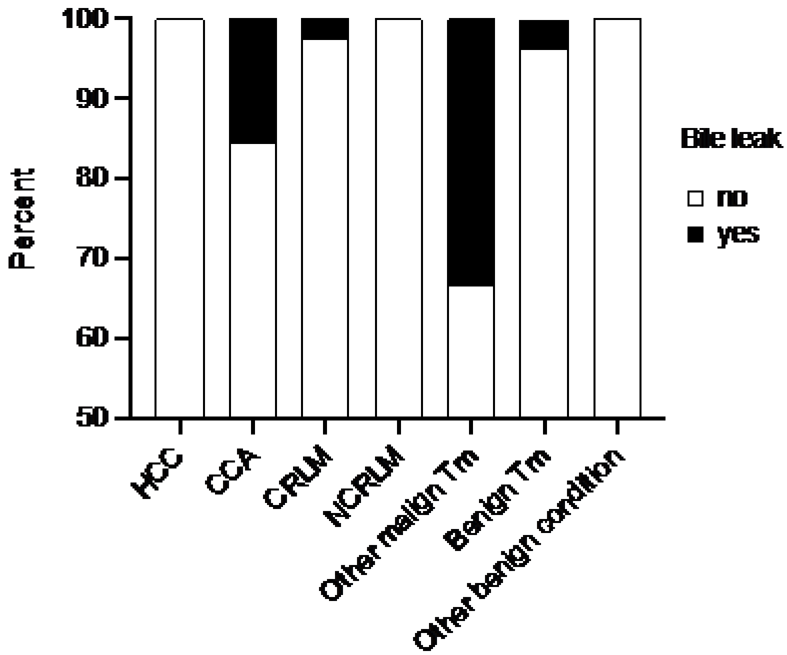

Figure 2

Rate of biliary leakage according to liver pathologies. CCA, cholangiocarcinoma; CRLM, colorectal liver metastases; HCC, hepatocellular carcinoma; nCRLM, non-colorectal liver metastases.

Supplementary Files

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