# Nodal Involvement

# 22

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## Introduction

Involvement of perihepatic lymph nodes (LN) does occur in patients with colorectal liver metastases (CLM), and is thought to originate from the liver metastases rather than the primary tumor [1, 2]. Most surgeons consider the presence of hepatic pedicle lymph node (HPLN) involvement (i.e., LN at the sites of hepato-duodenal ligament, retropancreatic area, common hepatic artery area, and coeliac axis area), and supradiaphragmatic, mediastinal, and para-aortic LN involvement as a contraindication for liver resection in patients with CLM. It has been regarded as equivalent to extrahepatic disease, essentially removing the chance of a curative liver resection. However, improvement of surgical procedures and recent developments of new chemotherapy regimens have led to reports of improved outcomes even in patients with HPLN involvement [3]. This book chapter presents a detailed description of hepatic lymph anatomy and distribution, the frequency and the clinical impact of HPLN involvement, and our surgical technique of en-bloc lymphadenectomy of HPLN. Its aim is to define the current clinical practice recommendations for patients with CLM and HPLN involvement based on the available evidence.

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## Anatomy

### Hepatic Lymph

The liver produces 25–50% of the entire lymphatic volume draining into the thoracic duct [4]. The hepatic lymphatic fluid originates from the hepatic sinusoids, and drains into each hepatic lymphatic vessel. The hepatic lymphatic vessels are divided into three categories depending on their location; portal, sublobular, and superficial lymphatic vessels [5]. At least 80%


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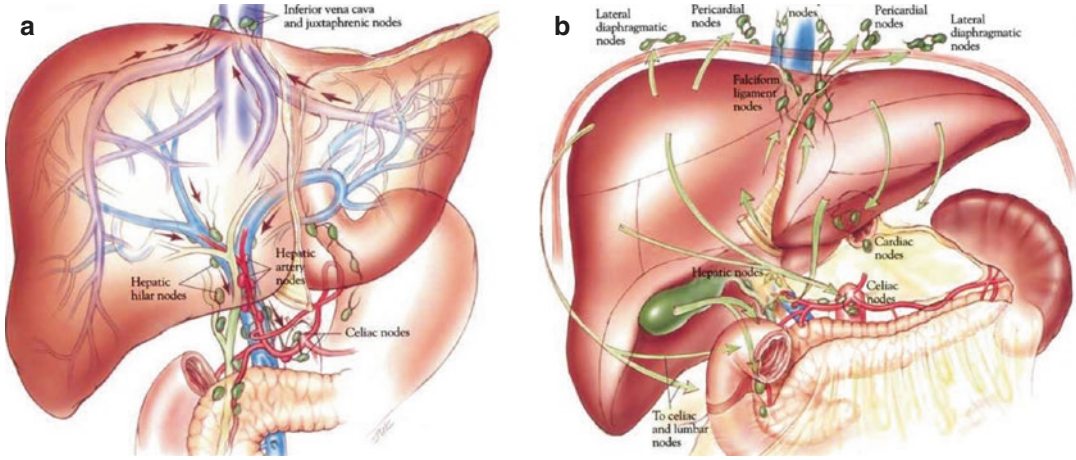



**Fig. 22.1** Schema of lymphatic drainage of the liver. Sublobular and portal lymphatic pathway (**a**) and superficial pathways (**b**) (Source: 'Patterns of spread of disease from the liver', Figs. 9 and 10; Meyers et al. Reprinted with the kind permission of Springer Science + Business Media, LLC) [31]

of hepatic lymphatic fluid drains toward the "porta hepatis" (i.e., transverse fissure of the liver), subsequently draining through lymphatic vessels in the hepatic pedicle (Fig. 22.1a). The remaining lymphatic fluid drains into either sublobular or superficial lymphatic vessels [5]. Sublobular lymphatic vessels drain into the inferior vena cava (Fig. 22.1a). The superficial lymphatic vessels form a complex capillary network under the liver capsule and drain into regional LN including supradiaphragmatic, mediastinal, and lesser omental LN (Fig. 22.1b) [6, 7].

## Drainage of Portal Lymphatic Vessels

According to cadaver studies of gallbladder lymphatics, the lymphatic drainage of the hepatic pedicle can be divided into three pathways: (1) the cholecysto-retropancreatic pathway (right descending pathway), (2) the cholecysto-celiac pathway (left oblique pathway), and (3) The cholecysto-mesenteric pathway (mesenteric pathway) [8, 9]. These three pathways converge with the para-aortic lymph nodes (PALN) near the left renal vein. The lymphatic vessels of the right descending pathway (to the right of the hepatoduodenal ligament) first drain into the cystic node and through several lymphatic vessels eventually into the epiploic foramen LN (foramen of Winslow), located to the right of the common hepatic duct (Fig. 22.2a). The epiploic foramen LN drains into the superior retropancreaticoduodenal (Rouvière) LN and from there either directly or via posterior pancreaticoduodenal LNs into the PALN at the level of the left renal vein (Fig. 22.2a). The lymphatic vessels of the left oblique pathway run along the cystic artery and hepatic artery to reach the nodes around the celiac trunk via the common hepatic artery (CHA) LN (Fig. 22.2b). The mesenteric pathway is composed of many thin lymph vessels originating from the porta hepatis and the gallbladder neck. These lymph vessels drain into the "principal portal node", located in front of the portal vein and at the confluence between portal vein and splenic vein. From this node, lymphatic vessels connect into LN surrounding the superior mesenteric artery (Fig. 22.2c). Several reports have argued that the right descending pathway is the dominant lymphatic pathway [10, 11].

In summary, the vast majority of hepatic lymphatic drainage is directed towards the HPLN.

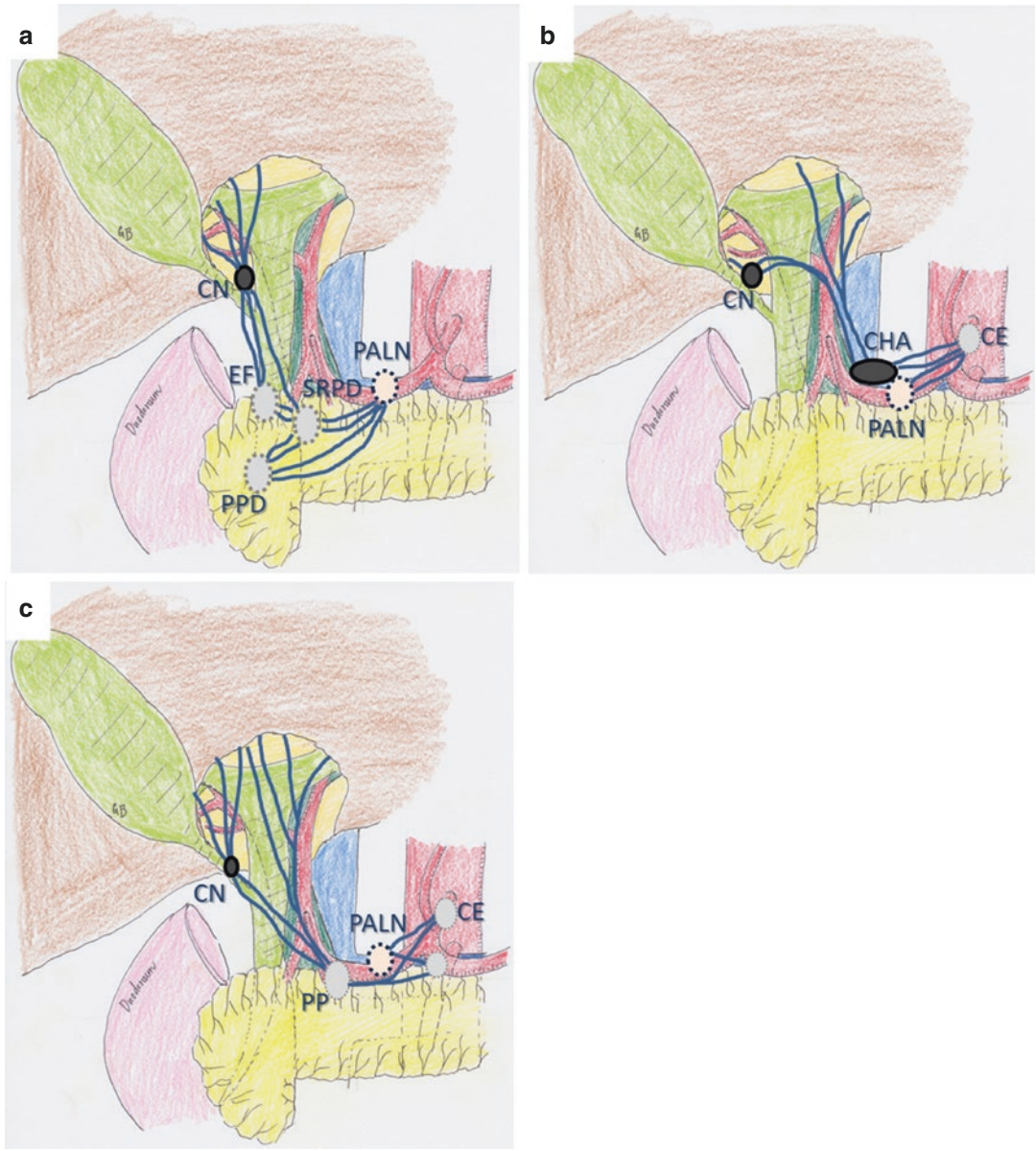



**Fig. 22.2** Schema of lymphatic vessels draining through hepatoduodenal ligament. (**a**) Right descending pathway; *CN*, cystic node; *EF*, epiploic foramen LN; *SRPD*, superior retro-pancreaticoduodenal LN; *PPD*, posterior pancreaticoduodenal LN; *PALN*, para-aortic LN. (**b**) Left oblique pathway; *CN*, cystic node; *CHA*, common hepatic artery LN; *CE*, celiac trunk LN; *PALN*, para-aortic LN. (**c**) Mesenteric pathway; *CN*, cystic node; *PP*, principal portal node; *CE*, celiac LN; *PALN*, para-aortic LN

## Frequency and Pre- and Intra-Operative Assessment of HPLN Involvement

The frequency of involvement of distant LN such as para-aortic, supradiaphragmatic and mediastitinal LN in patients with CLM is not well known. This is not surprising as lymph node dissection is rarely indicated and remains technically difficult. Interestingly the frequency of mediastinal LN involvement in colorectal cancer patients with lung metastasis was reported to be 12–33% [12, 13].

The analysis of HPLN involvement is further complicated by the fact that LN involvement can be either microsocpic or macroscopic. Studies looking only at macroscopic LN involvement, mostly by using the technique of "cherry picking", do not take into account the number of microscopically involved LNs and therefore may grossly underestimate the frequency of HPLN involvement. A few studies on the frequency of HPLN involvement are reliable, as they use systematic lymph node dissection in consecutive patients with microscopic analysis [14, 15]. The study from Beaujon Hospital [15] analyzed 76 patients who underwent systematic HPLN dissection simultaneously with CLM resection. Macroscopic palpable LN involvement (1 cm in a diameter and/or firm on palpation) was suspected in 23 patients during surgery. Of these, only ten patients had microscopically proven metastatic disease in the LN, and five patients who had microscopically node-positive disease were misdiagnosed as node-negative disease during surgery. In a series of 114 patients undergoing CLM resection reported by Elias et al. [14], 22 patients had microscopic HPLN involvement on final pathology, but only eight patients (40%) were suspected to have positive nodal disease intraoperatively.

**Table 22.1** Incidence of HPLN involvement in patients undergoing curative hepatic resection for CLM

| Authors | Year | Number of patients | Patients with nodal involvement |
|---|---|---|---|
| Nakamura [27] | 1999 | 79 | 7 (8.9%) |
| Jaeck [16] | 2002 | 160 | 17 (11%) |
| Elias [14] | 2003 | 114 | 22 (19%) |
| Laurent [28] | 2004 | 156 | 23 (15%) |
| Viana [29] | 2009 | 28 | 5 (17.9%) |
| Rau [15] | 2012 | 76 | 15 (20%) |

Therefore, the sensitivity and positive predictive value (PPV) of intraoperative diagnosis was quite low (67% and 43% respectively) [15]. In this context, frozen section analysis of macroscopically suspected LN would have less value. Current evidence suggests that accurate diagnosis of HPLN and other perihepatic LN involvement in patients with CLM during surgery is very difficult to obtain.

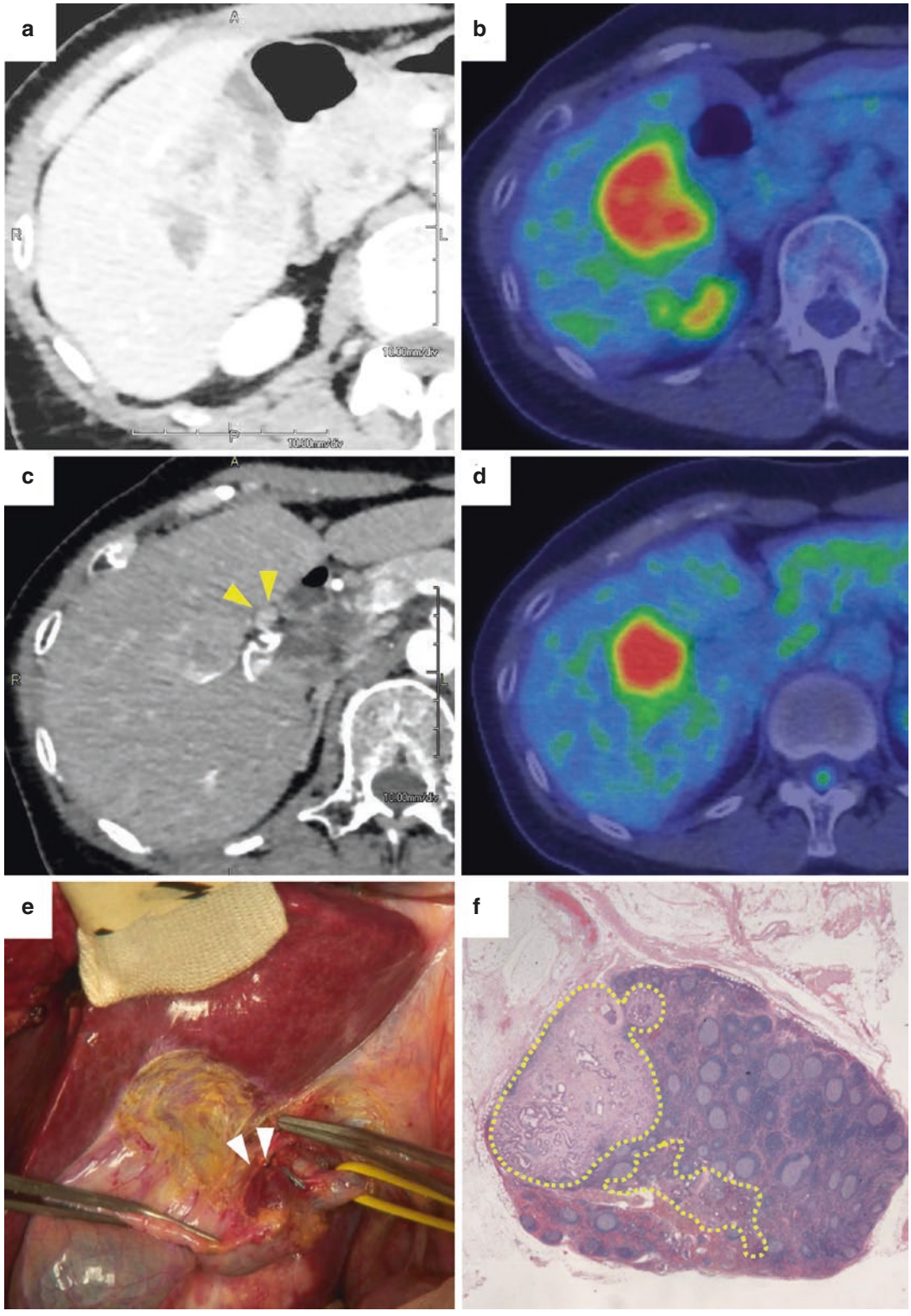
Studies using postoperative results of LN involvement after systematic HPLN dissection in patients with CLM report a frequency of 8.9–20% (Table 22.1). Elias et al. [14] studied the pattern of LN involvement in patients with CLM according to the anatomic location of respective LN basins. They divided LN specimens into six groups: (1) antero-superior LN in the hepatic pedicle, (2) antero-inferior LN in the hepatic pedicle, (3) postero-superior LN in the hepatic pedicle, (4) postero-inferior LN in the hepatic pedicle, (5) common hepatic artery LN, and (6) celiac LN. They showed that the most frequently invaded group of LNs was the common hepatic artery LN basin, and that the positive LN location was highly variable even in patients with a single CLM. This result suggests the possibility of "skip metastasis" and a random pattern of LN involvement in CLM patients.

The ability to predict the presence of HPLN involvement in patients with CLM was

evaluated by Jaeck et al. [16]. In this study the clinicopathological variables associated with HPLN involvement in 160 patients undergoing systematic HPLN dissection during liver resection for CLM were reviewed. Five relevant clinico-pathological factors were extracted by univariate analysis; (1) the presence of more than three CLM, (2) CLM located in segment 4 and / or segment 5, (3) synchronous CLM, (4) the presence of a resectable peritoneal deposit, and (5) poorly differentiated histology of CLM. In a similar study Elias et al. [17] evaluated 100 patients who underwent systematic HPLN dissection concomitantly with liver resection for CLM. They found that HPLN involvement was significantly correlated with (1) more than three metastases, (2) a greater than 15% tumor burden relative to total liver volume, and (3) a CEA level > 118 ng/L. In contrast, a study from the group at Beaujon Hospital with 76 patients who underwent systematic HPLN dissection simultaneously with liver resection for CLM (multiple CLM, 74%; bilobar CLM, 49%) did not find any correlation between HPLN involvement and any clinicopathological variables [15]. Based on these studies, it is reasonable to expect a higher chance of HPLN involvement in patients with higher tumor burden, multiple CLM, poor histology, and presence of extrahepatic disease.

Although very desirable, preoperative prediction of HPLN or other perihepatic LN involvement in patients with CLM remains very difficult. Current state-of-the-art imaging modalities such as 64-slice multi-detector computed tomography (MDCT), MRI, and PET scans lack sufficient diagnostic accuracy to be relied upon in clinical practice. The report from Beaujon Hospital team evaluated the ability of preoperative CT imaging to detect HPLN involvement compared to intraoperative assessment [15]. They defined preoperative LN involvement as greater than 1 cm in the short axis diameter, round-shaped, irregular contoured and/or heterogeneous LN in CT appearance. Of 15 patients with pathological proven LN involvement, only five patients fulfilled the preoperative imaging criteria for positive LN disease, resulting in a low sensitivity and positive predictive value (PPV) of 33% and 56% respectively. Positron emission tomography (PET) scan appears to be more accurate than CT for detection of HPLN involvement. A study from Memorial Sloan Kettering Cancer Center (MSKCC) evaluated 100 patients with metastatic hepatic malignancies who underwent liver resection and HPLN sampling [18]. In their study, CT scan had a high negative predictive value (NPV) of 95% and a low PPV of 39%, compared to PET scan with a NPV of 88% and a PPV of 100%. In patients demonstrating both a negative CT and PET scan, HPLN involvement was very unlikely (only one patient; 2.1%). However, systemic HPLN dissection was not performed, which limits the ability to assess the true denominator for occult metastases in this study and therefore prevents a true meaningful comparison of preoperative imaging and postoperative pathologic results. Although PET has a reasonable specificity for the presence of colorectal cancer and CLM (87%), it was found to be unreliable to detect LN metastases with a small tumor burden, leading to an overall low sensitivity of 37% for primary LN staging [19]. The authors experienced a CLM patient with HPLN involvement with a small tumor burden in whom both CT and PET scan were negative (Fig. 22.3a–f).

In conclusion, current imaging modalities cannot predict the presence of perihepatic LN involvement in patients with CLM with sufficient accuracy to be clinically valuable.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b
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f

## Prognosis of CLM Patients with Metastatic HPLN and Distant LN, Particularly Para-Aortic LN (PALN)

There have been few reports about the prognosis in patients with CLM and distant LN involvement. Two large studies analyzed the prognosis of CLM patients with resectable extrahepatic disease (EHD). An international multi-institutional database evaluated 1,629 patients with CLM who underwent resection for CLM [20]. Of these 1,629 patients, 171 (10.4%) had resectable EHD, and all malignant foci including CLM were removed. The common EHD sites were the lung ($n = 62$), HPLN ($n = 41$) and peritoneum ($n = 25$). PALN involvement was observed in 14 patients. The median survival and 5-year actual overall survival in patients without EHD who underwent CLM resection ($n = 1{,}458$) were 77 months and 57%, respectively, while the median overall survival was 39 months and 5-year overall survival rate was 26% in patients with successful resection of EHD. The prognosis of patients with HPLN involvement (median, 29 months; 5-year, 27%) was comparable to that of patients with lung metastasis (median, 46 months; 5-year, 33%) and peritoneal carcinomatosis (median, 32 months; 5-year, 26%). Patients with PALN involvement had a particularly poor survival (median, 13 months; 5-year, 7%). A second single institutional study evaluated 1,369 patients with CLM who underwent hepatic resection [21]. Of these, 127 (9%) underwent concomitant resection of EHD. The most common EHD site was the lung ($n = 34$) followed by HPLN ($n = 27$). Nine patients had ovarian metastasis. PALN and mediastinal LN involvement were observed in five patients and one patient respectively. The median and 5-year survival rate in 1,242 patients without EHD were 55 months and 49% respectively, compared to 36 months median survival and 26% 5-year survival in patients with EHD. Patients with HPLN involvement had poor survival (median, 26 months; 5-year, 12%), compared to 45 months median survival and 28% 5-year survival for patients with lung metastasis and 82 months median survival and 51% 5-year survival for patients with ovarian metastasis. The worst survival was seen in the five patients with PALN (median, 16 months). All five patients relapsed, and three of five patients died within 16 months of surgery.

Based on these results, concomitant resection of PALN may make little contribution to long-term survival, and patients found to have positive PALN probably should not undergo surgical resection upfront. Operation for those patients must be considered as palliative resections.

The prognosis of patients with HPLN involvement is not much better, based on the currently available evidence. A systematic review by Rodgers and McCall, published in 2000, reports the results of 15 English-language studies on the prognosis of patients who underwent concomitant CLM and HPLN resection [22]. Of 145 node-positive patients identified in this review, only five patients (3.4%) reached the 5-year survival point. The authors concluded that HPLN involvement constitutes a relative contraindication for CLM resection, similarly to other EHD. The ultimate success of operations in this context depends on the development of more effective multimodality treatment and chemotherapy regimen.

With the advent of modern multidrug chemotherapy for CLM and a better understanding of the location of HPLN metastases, recent data on

**Fig. 22.3** Clinical images of a 54-year-old female with metachronous solitary CLM and HPLN involvement in whom both CT and PET scans were negative. Preoperative CT scan indicates a 5.5 cm solitary CLM in the right hemi-liver (**a**), and fused PET/CT depicts a 2-[18F] fluoro-2-deoxy -D-glucose accumulation in the CLM (**b**). Preoperative CT scan; arrows indicate small HPLN of 7 mm in diameter located adjacent to the gallbladder (**c**). Fused PET/CT is negative for this small LN (**d**). **e** Intraoperative photography. *Arrows* indicate intraoperative gross appearance of LN. The LN was less than 1 cm in size and soft to palpation, suggesting a negative LN. It was removed with the gallbladder (**f**) and microscopic images (200×) revealed metastatic foci within the lymphatic tissues highlighted by the *dotted lines*

the prognostic implications of HPLN involvement on overall survival seems to indicate an improvement in outcome and patient selection. Two recent studies reported 5-year survival rates of more than 20% in patients with HPLN involvement [14, 20]. The study by Jaeck et al. from Strasbourg reported on 160 patients who underwent HPLN dissection simultaneously with curative liver resection for CLM [16]. They divided HPLN into two groups according to their specific anatomic location: area 1 = LN located at both hepatoduodenal ligament and retropancreaticoduodenal area, and area 2 = LN located at the site of the common hepatic artery and celiac axis. Of the160 patients analyzed, 17 had HPLN involvement. HPLN involvement limited to area 1 was found in eight patients, and HPLN involvement in area 2 was found in nine patients. No patient with area 2 involvement survived longer than 1 year after liver resection (3-year survival, 0%), whereas two of eight patients with area 1 involvement survived more than 3 years after surgery (3-year survival, 38%). Cognizant of the limitations for the small numbers, the authors concluded that currently liver resection for CLM in patients with area 2 HPLN involvement is definitively not justified. In a follow-up study, the same group analyzed 45 patients with HPLN involvement who underwent liver resection and concomitant dissection of HPLN [3]. HPLN involvement limited to area 1 or 2 was found in 17 and 18 patients respectively. Involvement of both areas was found in ten patients. The median survival and 5-year survival rate for all patients were 20.9 months and 17.3% respectively. There was no statistical difference of overall survival among the three groups of patients. On multivariate analysis, (1) serum CEA level $\geq$ 200 μg/L before liver resection, (2) R1 or R2 resection, (3) ratio of involved/resected HPLN = 1, and 4) absence of adjuvant chemotherapy were independent factors associated with poor overall survival. The 5-year survival rate in patients without any independent risk factor was 39.1%, whereas none of the patients with two or more risk factors reached the 2-year survival mark. These studies demonstrate that the ability to potentially select patients with favorable prognostic factors and the availability of multidrug effective chemotherapy may change the role of surgery in patients with perihepatic and, particularly HPLN involvement. The use of effective perioperative chemotherapy, as Rodgers and McCall had already noted, may be the most important factor to achieve acceptable survival rates after surgical resection in these patients.

## Surgical Technique of HPLN Dissection

There is no evidence that systemic routine en-bloc lymphadenectomy in patients undergoing CLM resection has prognostic value. Routine lymph node resection is not recommended in patients with CLM, since the majority of patients (>80%) are node-negative and the procedure fraught with potential complications, including ischemic bile duct stricture, pancreatic fistula, and lymphorrhea [23, 24]. On the other hand, en-bloc lymphadenectomy of HPLN might carry a benefit in selected patients who have enlarged HPLN on surgical exploration or on preoperative imaging, as enlarging HPLN can lead to obstructive jaundice, and determining the presence of metastatic disease has important prognostic value. Selected patients with long-term disease control after resection and adjuvant chemotherapy who develop metachronous disease in the HPLN following curative resection for CLM may also benefit from this procedure. It is important to rule out EHD in these patients prior to embarking on a possible regional lymphadenectomy.

Our technique of a standardized en-bloc lymphadenectomy of HPLN is described using a case of a 65-year-old male with intrahepatic cholangiocarcinoma. This patient underwent en-bloc lymphadenectomy of HPLN concurrent with central hepatectomy in National Hospital Organization, Kyoto Medical Center.

We prefer a bilateral subcostal incision with upper midline extension. After dissection and division of the round and falciform ligaments and generous Kocher's maneuver, the assistant subsequently retracts the duodenum anteriorly to expose the retropancreatic area (Fig. 22.4a).

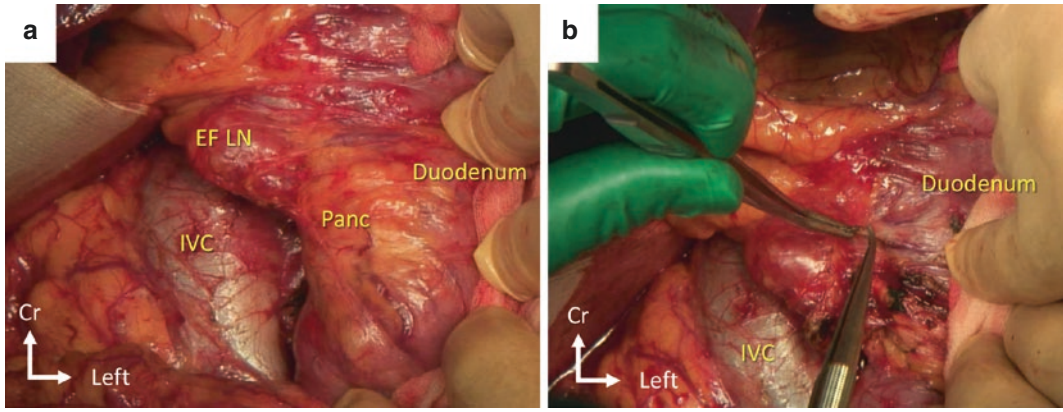



**Fig. 22.4** Intraoperative photographs of en-bloc lymphadenectomy of HPLN. (**a**) Preparation for retropancreatic LN dissection. *EF LN*, epiploic lymph node; *IVC*, inferior vena cava; *Panc*, pancreas. (**b**) Retropancreatic LN dissection is performed using pinch–burn–cut technique. *IVC*, inferior vena cava. (**c**) Right gastric artery is ligated and divided. *GB*, gallbladder. (**d**) Common hepatic artery (CHA) LN is retrieved up to the origin of left gastric and splenic arteries. *GDA*, gastroduodenal artery; *Panc*, pancreas. (**e**) *Arrowhead* indicates the origin of the right gastric artery, which arises from proper hepatic artery. *Arrow* indicates the stump of left gastric vein. *CHA*, common hepatic artery; *GDA*, gastroduodenal artery; *Panc*, pancreas; *PHA*, proper hepatic artery. (**f**) Complete dissection of the anterior border of the common hepatic artery (CHA) up to the origin of left gastric and splenic arteries. *GDA*, gastroduodenal artery; *Panc*, pancreas; *PHA*, proper hepatic artery; *CA*, celiac axis; *LGA*, left gastric artery. (**g**) The right side of celiac axis LN is dissected using ultrasonic scalpel. *CHA*, common hepatic artery; *GDA*, gastroduodenal artery; *PHA*, proper hepatic artery; *CA*, celiac axis; *LGA*, left gastric artery. (**h**) *Arrowheads* indicate left gastric vein which is ligated at the bifurcation of portal vein. *CHA*, common hepatic artery; *GDA*, gastroduodenal artery; *Panc*, pancreas; *PHA*, proper hepatic artery; *CA*, celiac axis; *LGA*, left gastric artery. *PV*, portal vein. (**i**) The *dotted lines* indicate the LNs of the left oblique pathway, which are separated from the left side and retracted to the patient's right. *CHA*, common hepatic artery; *GDA*, gastroduodenal artery; *CA*, celiac axis; *LGA*, left gastric artery. *PV*, portal vein. (**j**) LNs are dissected from the anterior border of portal vein using electrosurgical instrument. *CHA*, common hepatic artery; *GDA*, gastroduodenal artery; *CA*, celiac axis; *LGA*, left gastric artery. *PV*, portal vein. (**k**) The anterior border of the hepatoduodenal ligament is opened and left and middle hepatic arteries exposed. *CHA*, common hepatic artery; *GDA*, gastroduodenal artery; *PHA*, proper hepatic artery; *MHA*, middle hepatic artery; *LHA*, left hepatic artery. (**l**) LN dissection of left oblique pathway is completed. Traction of the PHA anterolaterally facilitates LN dissection of the posterior border of the hepatic arteries. *CHA*, common hepatic artery; *GDA*, gastroduodenal artery; *PHA*, proper hepatic artery; *LHA*, left hepatic artery; *PV*, portal vein; *LN*, lymph node. (**m**) *Arrowheads* indicate "3 o'clock" artery of CBD. During dissection, care should be applied to preserve these vessels. *GDA*, gastroduodenal artery; *PHA*, proper hepatic artery; *CBD*, common bile duct; *EF LN*, epiploic lymph node. (**n**) *Arrowheads* indicate a replaced right hepatic artery arising from the superior mesenteric artery. *CHA*, common hepatic artery; *GDA*, gastroduodenal artery; *MHA*, middle hepatic artery; *LHA*, left hepatic artery. *PV*, portal vein; *CBD*, common bile duct; *Panc*, pancreas. (**o**) *Arrowheads* indicate small arterial collaterals arising from a replaced hepatic artery. These small collaterals should be identified and ligated. *CHA*, common hepatic artery; *GDA*, gastroduodenal artery; *MHA*, middle hepatic artery; *LHA*, left hepatic artery. *PV*, portal vein; *CBD*, common bile duct; *Panc*, pancreas. (**p**) *Arrowheads* indicate the biliary stent inserted to perform intraoperative cholangiography. *CHA*, common hepatic artery; *GDA*, gastroduodenal artery; *MHA*, middle hepatic artery; *LHA*, left hepatic artery. *PV*, portal vein; *CBD*, common bile duct; *Panc*, pancreas. (**q**) *Arrowheads* indicate the posterior branch of the right hepatic artery. *Arrows* indicate the biliary stent inserted into the CBD via the cystic duct. *CHD*, common hepatic duct, *RHA*, right hepatic artery. (**r**) The area highlighted by the *dotted lines* indicates the right descending pathway LN, which is dissected from the hepatoduodenal ligament by a cranial–caudal approach. *CHA*, common hepatic artery; *GDA*, gastroduodenal artery; *LHA*, left hepatic artery. *PV*, portal vein; *CHD*, common hepatic duct; *Panc*, pancreas; *RHA*, right hepatic artery; *LN*, lymph node. (**s**) *Arrowheads* indicate the lymphatic vessels, which should be ligated before division. *PV*, portal vein; *CBD*, common bile duct; *Panc*, pancreas; *RHA*, right hepatic artery; *LN*, lymph node. (**t**) The area highlighted by the *dotted lines* indicates the retrieved LN, which are connected to the PALN located at the inferior border of left renal vein. The forceps grasps a part of PALN which has been divided. *GDA*, gastroduodenal artery; *PV*, portal vein; *CHD*, common hepatic duct; *Panc*, pancreas; *RHA*, right hepatic artery; *LN*, lymph node; *LRV*, left renal vein; *PALN*, para-aortic lymph node; *IVC*, inferior vena cava. (**u**) Completed lymphadenectomy. En-bloc lymphadenectomy of the HPLNs concurrent with central hepatectomy was completed. No blood transfusion was required. *GDA*, gastroduodenal artery; *PV*, portal vein; *CHD*, common hepatic duct; *Panc*, pancreas; *RHA*, right hepatic artery

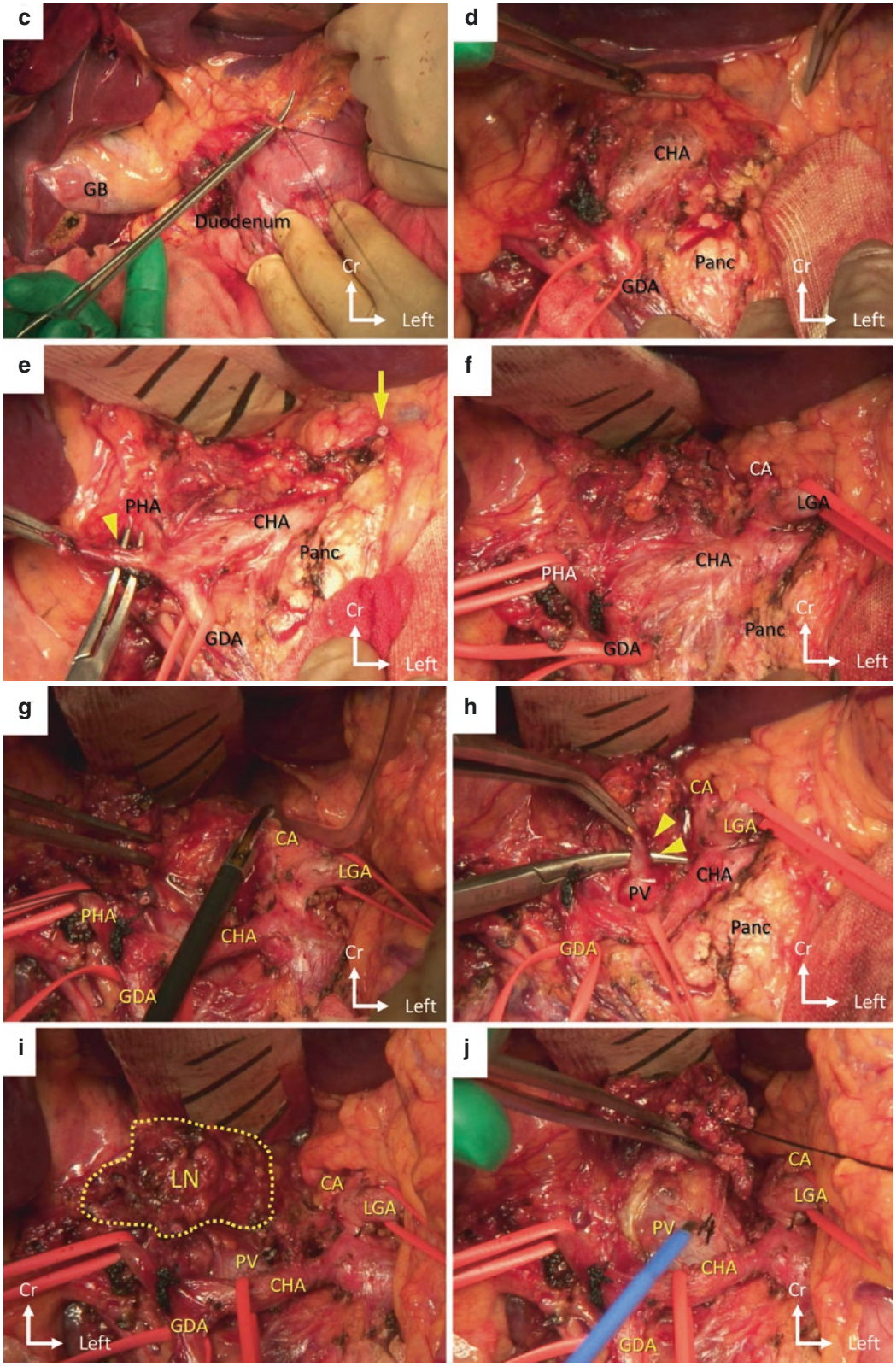
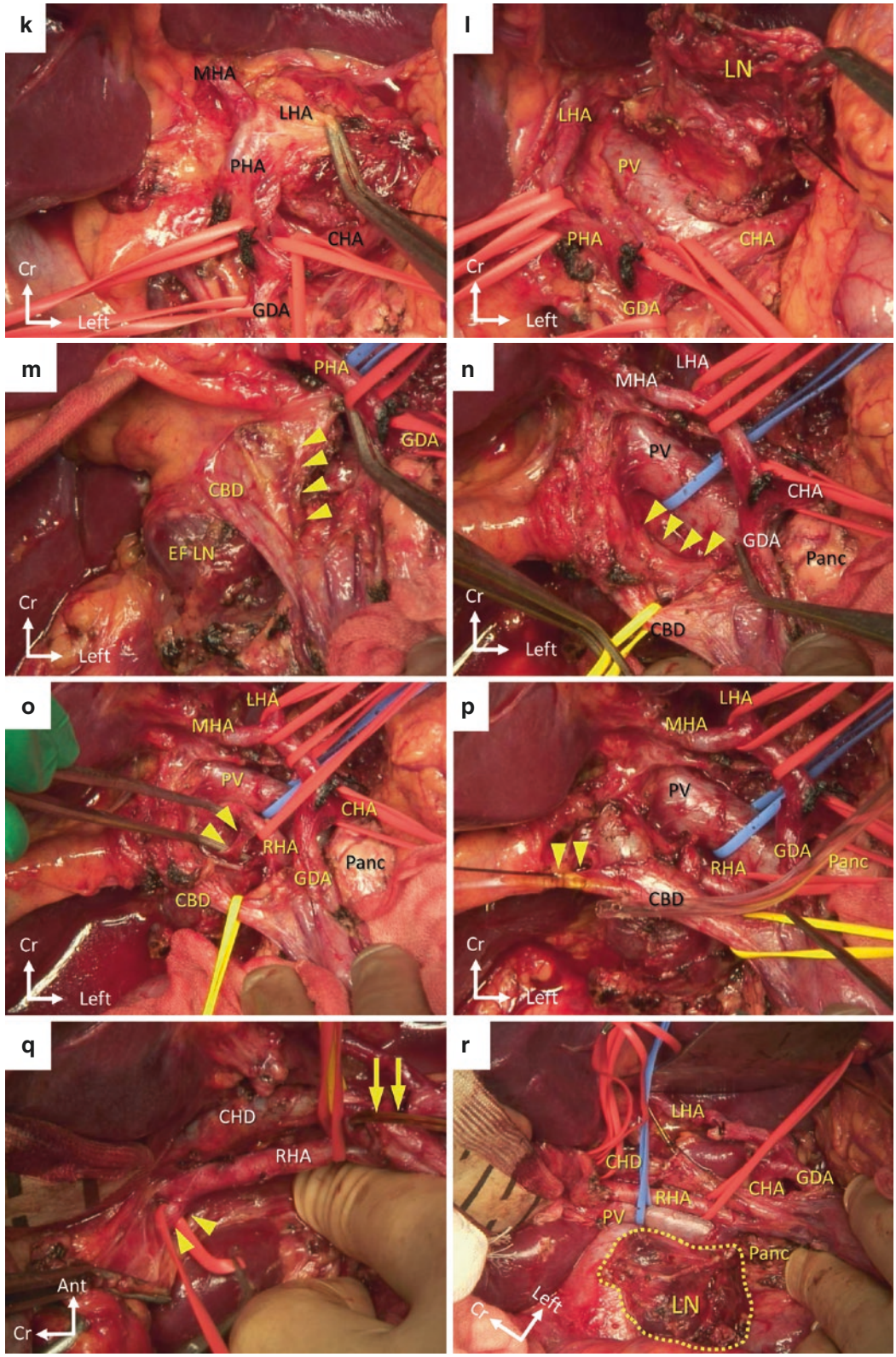



**Fig. 22.4** (continued)

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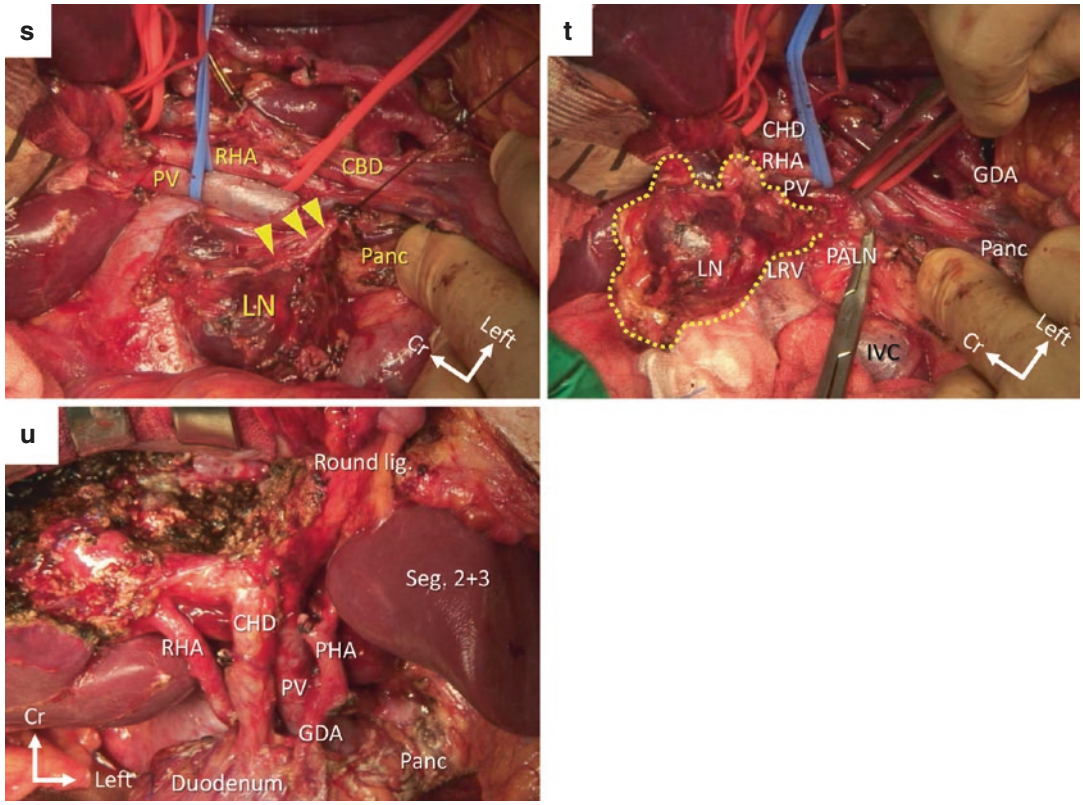


**Fig. 22.4** (continued)

The lymphadenectomy of the retropancreatic area is begun by harvesting the posterior pancreaticoduodenal and superior retropancreaticoduodenal LNs using the pinch–burn–cut technique (Fig. 22.4b) [25]. The peritoneal envelope of the hepatoduodenal ligament is transected at the upper border of the pancreatic head. Supraduodenal vessels should be preserved to maintain blood supply to the bile duct. The right gastric artery is ligated and divided (Fig. 22.4c), and the lesser omentum opened. The gastroduodenal artery is dissected and encircled with vascular tape. This exposes the lymphatic nodal tissue in front of the hepatic artery, which is cleared anterior and superior to the common hepatic artery (CHA) and up to the origin of the left gastric and splenic arteries (Fig. 22.4d and f). Care is taken not to injure the left gastric vein. If necessary, the vein can be ligated and divided to expose the posterior aspect of CHA (Fig. 22.4e). The LNs to the right of the celiac axis are dissected (Fig. 22.4g). Then CHA is encircled with vessel tape, and lymphadenectomy along its posterior surface is performed. The anterior surface of portal vein is exposed and the left gastric vein is ligated and divided (Fig. 22.4h). The celiac and CHA LN are completely separated from the left side and retracted to the patient's right (Fig. 22.4i). LNs are subsequently dissected from the anterior surface of the portal vein (Fig. 22.4j). The anterior surface of the left and middle hepatic arteries are exposed and circumferentially dissected using vessel tape (Fig. 22.4k). Anterolateral traction of these vessels allows clearance of the lymphatic tissue posterior to the proper and left hepatic arteries and to the left side of the portal vein (Fig. 22.3l). Lymphadenectomy on the right descending pathway is begun by dissecting the connective tissues around the common bile duct (CBD). The CBD is supplied via two main arteries running at the left and right border of the bile duct, the "3

**Table 22.2** Review of publications describing prognostic implications of HPLN involvement on overall survival

| Authors | Year | Number of patients | Patients with nodal involvement | 5-year overall survival rate | |
|---|---|---|---|---|---|
| | | | | HPLN (+) | HPLN (−) |
| Jaeck [16] | 2002 | 160 | 17 (11%) | 0 | 47% |
| Elias [14] | 2003 | 385 | 12 (3%) | 27% | NR |
| Laurent [28] | 2004 | 156 | 23 (15%) | 5% | 43% |
| Adam [30] | 2008 | 763 | 47 (6%) | 18% | 53% |
| Carpizo [21] | 2009 | 1369 | 27 (2%) | 12% | 49% |
| Oussoultzoglou [3] | 2009 | 45 | 45 (100%) | 17.3% | NR |
| Pulitano [20] | 2012 | 1629 | 41 (3%) | 27% | 57% |

*HPLN* hepatic pedicle lymph node; *NR* not reported

o'clock" and "9 o'clock" arteries, which variably arise from the retroportal, retroduodenal or gastroduodenal arteries and communicate with the right or less often with the left hepatic artery [26]. Therefore, dissection should be done with caution to avoid injury to these vessels (Fig. 22.4m). The CBD is subsequently encircled and retracted laterally to facilitate identification of a replaced right hepatic artery (Fig. 22.4n). The dissection is carried out between the right hepatic artery and CBD. Small arterial collaterals should be identified and ligated in order to avoid subadventitial hemorrhage (Fig. 22.4o). After identification of the cystic duct, a biliary stent is inserted into the CBD through the cystic duct to perform intraoperative cholangiography (Fig. 22.4p). Lymphadenectomy is continued by harvesting the cystic node and dissecting the "porta hepatica". This procedure allows exposure of the anterior border of the common hepatic duct and right hepatic artery. The dissection is continued until the posterior branch of right hepatic artery is identified and encircled with vascular tape (Fig. 22.4q). The LNs along the posterior border of the hepatoduodenal ligament are retrieved by exposing the posterior border of the right hepatic artery and portal vein. The dissection is continued inferiorly to the epiploic foramen LNs which are harvested. Dissection is carried on to the upper and posterior border of the head of the pancreas, harvesting any encountered LNs (Fig. 22.4r). All visible lymphatic vessels should be ligated to prevent postoperative lymphorrhea (Fig. 22.4s). En-bloc lymphadenectomy of HPLN ultimately ends by division of the connection to the PALN (Fig. 22.4u). After completion of the procedure, the hepatoduodenal ligament is completely devoid of lymphatic tissue and LNs. Between April 2012 and May 2015, we performed 14 en-bloc lymphadenectomies of the HPLN, with a mean number of 13 LNs retrieved per patient (range, 3–22). All patients had biliary tract cancer including gallbladder cancer and intrahepatic cholangiocarcinoma and underwent en-bloc lymphadenectomy concurrent with liver resection without biliary reconstruction. There was no mortality and no specific postoperative complication related to the LN dissection. Overall morbidity rate was 7.1% ($n$ = 1), including an organ/space surgical site infection requiring antibiotic therapy.

Safe and successful en-bloc lymphadenectomy of HPLN can be achieved by paying attention to the following steps: avoid injury (1) to the small arterial collaterals during the LN dissection adjacent to the named arteries to avoid subadventitial hemorrhage leading to arterial thrombosis, (2) to the pancreas to prevent pancreatic fistula, and (3) to the supraduodenal vessels and the "3 o'clock" and "9 o'clock" arteries during the common bile duct dissection to prevent ischemic bile duct strictures. All the visible lymphatic vessels should be ligated in order to prevent postoperative lymphorrhea. The maintenance of an appropriate dissecting plane between LN and the structures of hepatic pedicles is of upmost importance to achieve safe en-bloc lymphadenectomy.

## Conclusions

In patients with CLM, HPLN involvement has been one of the most powerful prognostic factors associated with poor survival after

liver resection. Patients with primary colorectal cancer who have regional LN involvement can achieve long-term survival by means of regional lymphadenectomy concomitant with resection of the primary tumor, while surgical resection alone has not improved prognosis of patients with CLM who have HPLN involvement. The biologic relevance of lymphatic invasion in patients with CLM can be viewed as equivalent to systemic disease. Therefore, if metastatic disease is suspected or proven in HPLN, surgical resection should only be entertained in the context of a multimodality treatment algorithm. Despite advances in imaging modalities, it remains very difficult to identify HPLN involvement preoperatively in those 20% of patients having metastatic HPLN disease. The prognostic and therapeutic implications of systematic routine en-bloc lymphadenectomy of HPLN remain unclear and need further investigation. With improved systemic treatment options, surgical removal of involved HPLN nodes may translate into a survival advantage in selected patients with PET-positive nodes and after curative resection with long-term response to chemotherapy, but at this time cannot be viewed as standard of care.

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