Two-Stage Liver Surgery

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Although surgical resection is still the only treatment that can provide prolonged survival and a hope of cure for patients with colorectal liver metastases (CLM), nearly 80% of patients with CLM are thought not to be resectable at the time of diagnosis [1–3]. These patients were traditionally considered for palliative chemotherapy. Hence, to increase resectability for those patients is an issue of great importance.

In order to overcome the initial unresectability, considerable efforts have been made during the last two decades. The advent of more effective chemotherapy and developments of surgical procedure and perioperative management have expanded the pool of resectable patients with CLM, and a certain number of patients with initially unresectable CLM can be converted to resectable and have a chance of prolonged survival [4–9]. However, even with effective chemotherapy with or without targeted therapy, conversion rate is reported to be only 20% [9].

For patients with extensive bilateral multinodular CLM, a single hepatectomy, even with specific procedures such as portal vein embolization (PVE) and local ablation therapy is sometimes not sufficient to remove all the tumors, even after significant downsizing by chemotherapy. In 2000, our team reported the concept of two-stage hepatectomy (TSH), based on two sequential procedures to remove multiple bilateral tumors impossible to remove by a single hepatectomy, and using the liver regeneration obtained after the first procedure [10]. During the next decade, this procedure has evolved in combination with PVE and effective chemotherapy, and has been adopted by many specialized centers worldwide with promising short- and long-term outcomes. Herein, we describe the history, surgical technique, indication, drawbacks and outcomes of TSH for CLM.

Introduction and Development of TSH

The concept of TSH was first introduced by our team, in order to treat the patients with multiple bilateral unresectable metastases, since 1992 and published in 2000 [10]. Of note, the indication of this strategy was only bilateral, multinodular tumors which were unable to be resected by a single hepatectomy, even in combination with preoperative chemotherapy and with specific procedures such as PVE and local ablation therapy. This strategy aimed to remove all the intrahepatic tumors sequentially, by

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inducing hypertrophy of the future liver remnant (FLR) before second-stage hepatectomy, to avoid the risk of postoperative liver failure. In this first series, 6 of 13 patients who completed TSH received additional PVE to obtain more sufficient FLR hypertrophy [10]. Subsequently, the team of Strasbourg developed TSH, with routine use of PVE after first-stage and sequential right (or extended right) hepatectomy [11]. Since then, many specialized centers have adopted, developed, and modified this strategy.

Indication of TSH for CLM

Indication of TSH for CLM at Paul Brousse Hospital is summarized in Fig. 13.1. When the multinodular tumors are unilobar and thought to be unresectable because of small FLR (usually less than 30% or 40% when patients received prolonged chemotherapy), we perform PVE followed by one-stage hepatectomy (Fig. 13.1a). When the multinodular tumors are bilobar but the largest tumor size is ≤30 mm and the tumor number in the FLR ≤3, we generally perform standard one-stage hepatectomy with simultaneous local ablation therapy (Fig. 13.1b). When the multinodular tumors are bilobar, the largest tumor size is >30 mm, and/or the tumor number in the FLR >3, in the FLR, we consider TSH (Fig. 13.1c). In the literature, 3–29% of the patients with CLM who were submitted to surgery were planned for TSH (Table 13.1).

Concomitant Extrahepatic Disease

Previous studies reported the rate of concomitant extrahepatic disease to be ranged from 0 to 33% in patients who were planned for TSH (Table 13.2). At Paul Brousse Hospital, the presence of extrahepatic metastases is not considered a contraindication for hepatectomy if these are limited and resectable. When limited extrahepatic disease is located in the abdominal cavity (i.e. pedicular lymph node or peritoneal metastases), resection is performed at the time of first-stage hepatectomy. When extrahepatic

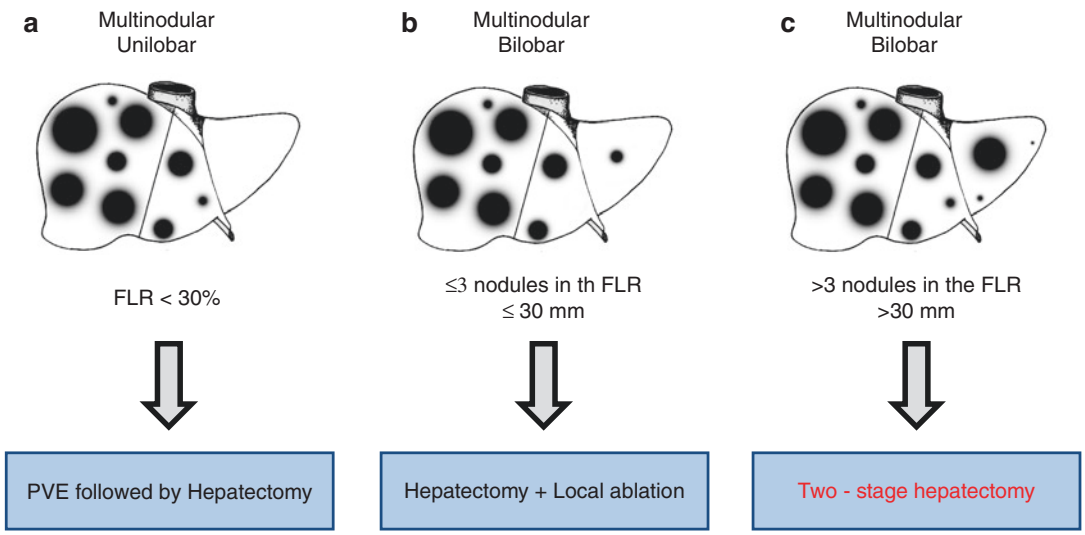

Fig. 13.1 Indication of two-stage hepatectomy for colorectal liver metastases at Paul Brousse Hospital. (**a**) When the multinodular tumors are distributed unilobar and thought to be unresectable because of small future liver remnant (FLR), portal vein embolization (PVE) followed by one-stage hepatectomy is performed. (**b**) When the multinodular tumors are distributed bilobar but the largest tumor size is ≤30 mm and the tumor number in the FLR ≤3, standard one-stage hepatectomy with simultaneous local ablation therapy is performed. (**c**) When the multinodular tumors are distributed bilobar, the largest tumor size is >30 mm and the tumor number in the FLR >3, two-stage hepatectomy (TSH) is performed

Table 13.1 Demographics of studies of two-stage hepatectomy for colorectal liver metastases in the literature

Study	Year	Country	Study periods	Total No. of surgically treated pts. for CLM	No. of pts. planned for TSH	Percentage of pts. planned for TSH (%)
Lygidakis et al.	2004	Greece	1991–2003	NR	62	NR
Garcea et al.	2004	UK	2001–2003	446	11	3
Pamecha et al.	2008	UK	1999–2005	280	14	5
Homayounfar et al.	2009	Germany	2005–2007	NR	24	NR
Tsai et al.	2010	USA	1994–2008	720	45	6
Karoui et al.	2010	France	2000–2008	NR	33	NR
Tsim et al.	2011	UK	2003–2006	131	38	29
Brouquet et al.	2011	USA	2002–2010	890	65	7
Narita et al.	2011	France	1996–2009	753	80	11
Stella et al.	2012	France	1995–2009	1042	56	5
Bowers et al.	2012	UK	2004–2010	NR	33	NR
Tanaka et al.	2012	Japan	2003–2011	232	24	10
Turrini et al.	2012	France	2000–2010	NR	48	NR
Muratore et al.	2012	Italy	1997–2009	653	47	7
Cardona et al.	2014	USA	2000–2009	1188	40	3
Giuliante et al.	2014	Italy	2002–2011	NR	130	NR
Faitot et al.	2015	France	2004–2010	NR	50	NR
Imai et al.	2015	France	2000–2012	845	125	15

When multiple publications were identified from the same institutions, only the most recent publication was included.
CLM colorectal liver metastases, *TSH* two-stage hepatectomy, *NR* not reported

Table 13.2 Perioperative features at first-stage hepatectomy

	Concomitant extrahepatic disease (%)	Preoperative chemotherapy (%)	Simultaneous resection of primary tumor (%)	Major resection (%)	Concomitant use of local ablation therapy (%)	Intraoperative PVE/PVL (%)	Morbidity (%)	Mortality (%)
Lygidakis et al.	NR	NR	100	0	100	100	11	0
Garcea et al.	0	100	0	28	0	NR	NR	0
Pamecha et al.	0	100	0	14	0	0	0	0
Homayounfar et al.	4	75	0	0	29.2	100	13	0
Tsai et al.	7	71	49	25	23	73	26	4
Karoui et al.	12	61	100	0	15	52	21	0
Tsim et al.	0	97	0	NR	0	0	11	0
Brouquet et al.	0	100	29	3	3	0	25	0
Narita et al.	14	84	31	0	32	4	14	0
Stella et al.	6	96	49	4	76	61	37	0
Bowers et al.	0	85	31	23	9	3	23	0
Tanaka et al.	33	100	NR	5	0	86	29	0
Turrini et al.	0	100	37	0	67	0	10	0
Muratore et al.	26	79	0	4	0	23	19	0
Cardona et al.	0	100	100	2	9	9	14	0
Giuliante et al.	26	87	55	3	4	52	17	0
Faitot et al.	10	90	NR	NR	38	88	18[a]	2
Imai et al.	26	98	30	2	10	76	14[a]	1

[a]Major complication (Clavien ≥ III)
PVE portal vein embolization, *PVL* portal vein ligation, *NR* not reported

disease is located outside the abdomen (such as lung metastasis), resection is usually performed 2–3 months after the second-stage hepatectomy, provided that the disease remains controlled by chemotherapy. In our recent study (2000–2012), concomitant extrahepatic disease was observed in 26% of the patients who were planned for TSH [12]. Among them, resection of concomitant extrahepatic disease was consequently achieved in 42%. Remaining concomitant extrahepatic disease was not resected mainly because of disease recurrence after second-stage hepatectomy or in cases of TSH failure. In our treatment strategy, the presence of extrahepatic disease was neither a predictive factor of TSH failure nor a prognostic factor of survival after TSH (unpublished data). What is crucial however, is to envisage resection of concomitant extrahepatic disease when the disease is controlled by chemotherapy.

Surgical Procedures of TSH

First-Stage Hepatectomy

At Paul Brousse Hospital, during the first-stage hepatectomy, either the most invaded hemiliver (usually the right) is resected, or, in most cases, the less-invaded liver lobe (FLR) is cleared of its metastases [10, 12, 13]. In the literature, limited hepatectomy (<3 segments) was mainly performed during first-stage hepatectomy (Fig. 13.2). Clearance is generally obtained by non-anatomical resection (Fig. 13.2a), and local ablation therapy such as cryotherapy and radiofrequency ablation (RFA), is only used in combination with hepatectomy for the treatment of unresectable tumors deeply located in the FLR with the purpose of sparing liver parenchyma of the FLR. Portal vein ligation (PVL)/PVE is routinely performed intraoperatively during the

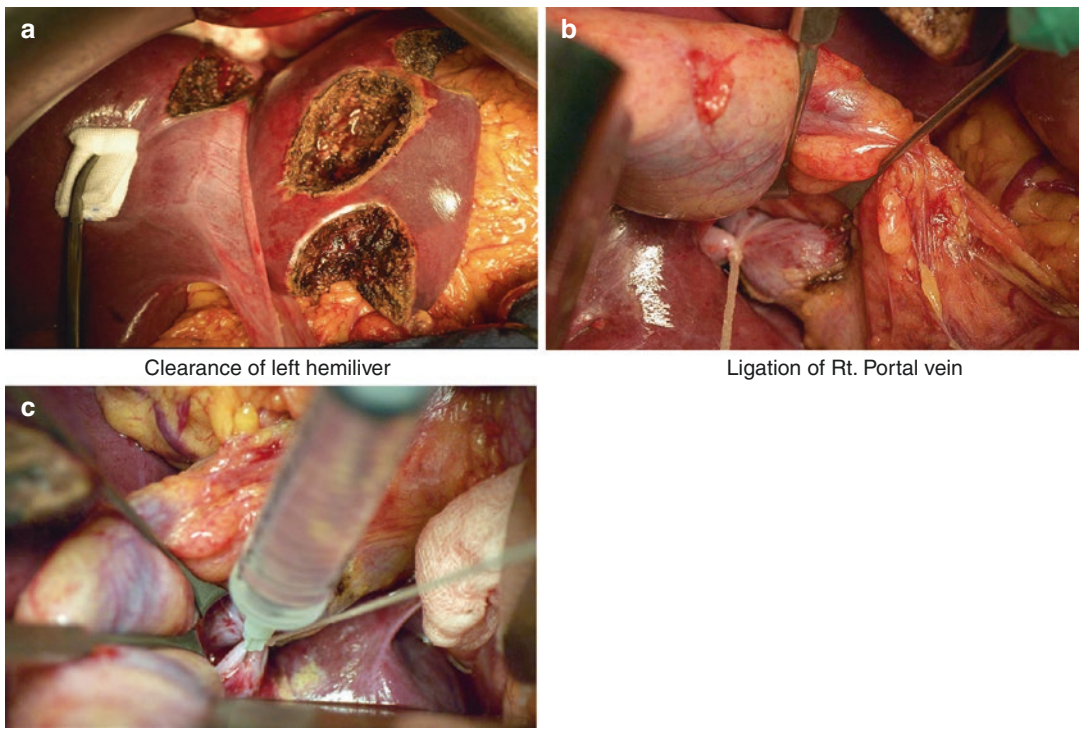

Fig. 13.2 Procedure of two-stage hepatectomy. (**a**) During the first-stage hepatectomy, in most cases, the less-invaded liver lobe is cleared of its metastases, usually by non-anatomical resection. (**b**) Ligation of right portal vein. (**c**) Embolization by dehydrated ethanol. For the safety of second-stage hepatectomy, portal vein ligation and embolization is routinely performed during first-stage hepatectomy

first-stage. Previous studies reported that stimulation of liver hypertrophy could also accelerate intrahepatic tumor progression after PVE [14–17]. From this aspect, what is essential during first-stage hepatectomy is that all tumors in the FLR should be removed to avoid tumor regrowth, leading to the failure to proceed to second-stage procedure.

Portal Vein Ligation/Embolization

At Paul Brousse Hospital, for the safety of second-stage hepatectomy, PVE using dehydrated ethanol in combination with ligation is routinely performed during first-stage hepatectomy (about 82%) (Fig. 13.2b, c) [12]. If PVL/PVE is not performed during first-stage, percutaneous PVE is added after first-stage (about 18%). The volume of FLR is evaluated by volumetric computed tomography (CT) analysis 4–6 weeks later. Whether PVL/PVE is performed during or after first-stage hepatectomy seems to depend on institutions (Tables 13.2 and 13.3).

Second-Stage Hepatectomy

Second-stage hepatectomy is performed when: (1) curative resection is possible, (2) the remaining disease is controlled by chemotherapy, and (3) the volume of FLR is thought to be sufficient. When the most invaded hemiliver is resected during first-stage, tumor clearance is performed from the remnant liver, usually by non-anatomical partial resection. When, in most cases, the less-invaded liver lobe is cleared of its metastases during first-stage, the tumor-bearing liver lobe is anatomically removed (usually lobectomy or extended lobectomy). In the literature, major hepatectomy (≥3 segments) was mainly performed during second-stage hepatectomy (76–97%) (Table 13.3).

Concomitant Use of Local Ablation Therapy

Local ablation therapy including cryotherapy and RFA is only used in combination with hepatectomy for the treatment of unresectable tumors

Table 13.3 Perioperative features at second-stage hepatectomy

	Interval duration (days)	Interval PVE (%)	Interval chemotherapy (%)	Major hepatectomy (≥3 segments) (%)	Concomitant use of local ablation therapy (%)	Morbidity (%)	Mortality (%)
Lygidakis et al.	40	0	100	77	0	11	3
Garcea et al.	150	NR	0	78	0	33	0
Pamecha et al.	210	35.7	100	73	0	27	0
Homayounfar et al.	42	0	0	73	11	58	5
Tsai et al.	135	4	62	80	17	26	6
Karoui et al.	111	15	76	92	4	32	4
Tsim et al.	NR	95	13	NR	0	33	0
Brouquet et al.	32	70	19	85	0	49	0
Narita et al.	92	92	31	95	8	54	0
Stella et al.	NR	0	84	92	12	49	0
Bowers et al.	84	72	15	59	7	56	4
Tanaka et al.	NR	0	52	76	0	38	0
Turrini et al.	72	100	29	91	59	20	6
Muratore et al.	114	56	53	94	0	44	0
Cardona et al.	150	60	86	83	30	60	0
Giuliante et al.	39	48	30	97	NR	35	4
Faitot et al.	NR	0	32	NR	NR	NR	NR
Imai et al.	96	16	74	93	6	33	3

PVE portal vein embilization

deeply located in the remnant liver, as described above. Recent systematic review reported that concomitant local ablation therapy such as cryotherapy, microwave or RFA, was performed in 17% (range, 0–67%) at first-stage and in 12% (range, 0–59%) at second-stage, respectively (Tables 13.2 and 13.3) [18]. At Paul Brousse Hospital, between 2000 and 2012, concomitant local ablation therapy was performed in 9.6% (12/125) at first-stage and in 6.2% (5/81) of patients at second-stage, respectively, and concomitant use of local ablation therapy did not influence the failure of TSH and the short-term outcome [12]. Furthermore, long-term outcome after TSH is also not affected by the concomitant use of local ablation therapy (unpublished data).

Primary Tumor Resection in Case of Synchronous Presentation

If the primary tumor is synchronous presented, its resection is performed at the time of first-stage hepatectomy or after second-stage hepatectomy. A Recent review reported that simultaneous resection of primary tumor was performed in a median proportion of 30% at first-stage hepatectomy [19]. However, whether or not the resection of primary tumor is performed during first-stage hepatectomy (when still in place) seems to depend on institutions (Table 13.2). In our recent study between 2000 and 2012, 46% of the patients who were planned for TSH had primary tumor in place at the moment of first-stage hepatectomy [12]. Among them, 66% underwent simultaneous colorectal resection during the first-stage, while 19% did so after the second-stage hepatectomy. Colorectal resection could not be performed on remaining 16% of the patients either because of failure of TSH or hepatic recurrence after second-stage hepatectomy. Previous studies reported that simultaneous resection of the primary tumor with first-stage hepatectomy did not affect the postoperative course [20, 21] and has the advantage to, reduce the number of procedures and optimize administration of chemotherapy [20].

Chemotherapy

Preoperative Chemotherapy

Preoperative chemotherapy is administered in almost all the cases before TSH in most institutions including ours (Table 13.2). We evaluated with CT, the response to chemotherapy after every four cycles of treatment, according to the Response Evaluation Criteria in Solid Tumors criteria [22]. In principal, hepatectomy is performed when the tumors are responding to chemotherapy (or at least in case of stable disease). In our recent update, disease progression during first-line chemotherapy and preoperative chemotherapy cycles >12 were the independent predictive factors of failure of TSH, together with carcinoembryonic antigen (CEA) >30 ng/mL and tumor size >40 mm. If we consider performing TSH for patients with extensive CLM, optimal first-line chemotherapy with short duration is crucial to prevent the failure of TSH [12].

Interval Chemotherapy

To decrease the drop-out rate from second-stage because of disease progression between the two stages, we generally recommend interval chemotherapy. Interval chemotherapy is delivered 3 weeks after first-stage hepatectomy using the same regimen as that used before first-stage hepatectomy. In our recent study, however, although nearly three fourth of the patients received interval chemotherapy, the interval chemotherapy failed to decrease the rate of TSH failure [12]. Another study also reported that interval chemotherapy could not decrease the failure rate of TSH [23]. We should also take into account the risk of liver injury by prolonged chemotherapy. To our knowledge, there is no study demonstrating the evidence of efficacy of interval chemotherapy for the feasibility or for survival. Thus the efficacy of interval chemotherapy is still uncertain and needs to be validated.

Postoperative Chemotherapy

At Paul Brousse Hospital, chemotherapy after second-stage hepatectomy is routinely recommended, if the patients' condition allows. Our previous study demonstrated that postoperative chemotherapy was an independent prognostic factor of survival after TSH [13]. However, recent update of our data failed to demonstrate the efficacy of postoperative chemotherapy on survival after TSH by multivariate analysis (only by univariate analysis, unpublished data). Therefore, the usefulness of routine postoperative chemotherapy (adjuvant setting) still needs to be demonstrated.

Drawbacks of TSH

The main drawback of TSH is obviously the failure to complete both two sequential procedures. Recent systematic review reported that failure rate of TSH ranges 0–36% (median, 23%), and the main reason of failure was disease progression between the two stages (56–100%, median, 100%) [19]. At Paul Brousse Hospital, between 2000 and 2012, 125 patients with initially unresectable, multiple, bilobar CLM were scheduled to undergo TSH. Among them, 44 patients could not proceed to second-stage (failure rate 35.2%). The reasons of failure of TSH were tumor progression in 39 patients (intrahepatic: 20, extrahepatic: 13, both: 6), insufficient volume of FLR in 3, poor general condition in 1, and postoperative mortality in 1 [12]. The overall survival (OS) after first-stage hepatectomy for patients who failed TSH was significantly lower than those who complete TSH (1, 3, 5-year OS rate: 66.3%, 14.0% and 0% vs. 95.0%, 69.0%, and 44.2%, $P < 0.0001$, Fig. 13.3) [12]. Therefore, to prevent the failure of TSH is crucial for patients who are planned for TSH, and this requires the prevention of disease progression after first-stage hepatectomy.

One possibility to prevent disease progression after first-stage is interval chemotherapy. However, there is little evidence supporting the routine use of interval chemotherapy in terms of preventing failure of TSH, as mentioned above. In addition, prolonged chemotherapy may lead to increase postoperative complications such as postoperative liver failure [24, 25]. Regarding interval chemotherapy, further large-scale study will be necessary.

In the literature, some predictive factors for failure of TSH have been reported (Table 13.4) [12, 26–30]. Recently, we identified four independent predictive factors for failure of TSH (Tumor progression on first line chemotherapy, number of chemotherapy cycles >12,

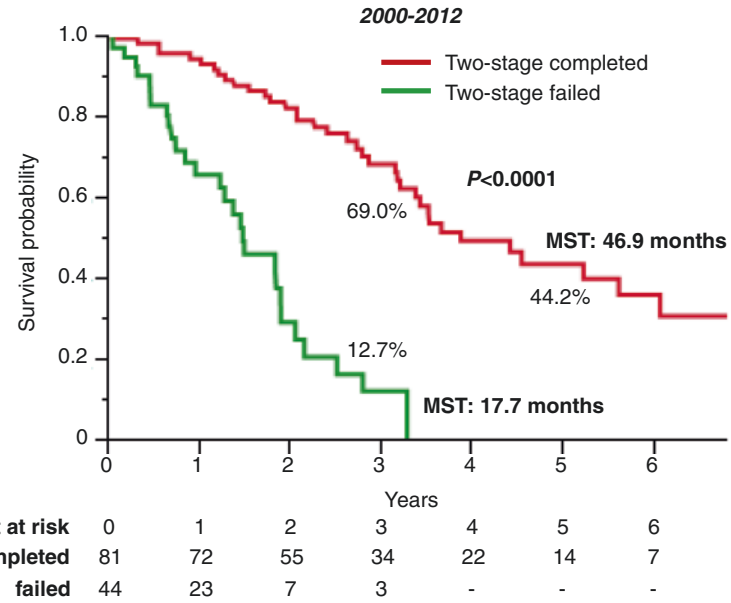

Fig. 13.3 Overall survival for patients who completed two-stage hepatectomy ($n = 91$) or failed ($n = 44$), between 2000 and 2012. *MST* mean survival time

Table 13.4 Reported predictive factors for failure of two-stage hepatectomy

Study	Year of publication	Country	No. of pts	Failure rate (%)	Predictive factors for failure of TSH	
					Univariate	Multivariate
Tsai et al.	2010	USA	45	22	• Higher tumor number • No preoperative chemo	• ND
Narita et al.	2011	France	76	20	• Age ≥ 70 • ≥3 tumors in the FLR • CEA > 200 (ng/mL) before PVE	• Age ≥ 70 • ≥3 tumors in the FLR
Turrini et al.	2012	France	42	19	• Combined resection of primary tumor • Interval chemotherapy	• Combined resection of primary tumor
Giuliante et al.	2014	Italy	126 (multicenter)	22	• Disease progression during chemo	• Disease progression during chemo
Faitot et al.	2015	France	50	24	• Male gender • Vascular invasion on primary • >5 tumors • Segment 1 metastases • Need for chemo change • Need for >3 curative treatments • Microscopic biliary invasion	• Nothing
Imai et al.	2015	France	125	35	• CEA > 30 (ng/mL) • Tumor size > 40 (mm) • No. of chemotherapy cycles > 12 • No. of chemotherapy lines > 1 • Disease progression during first-line chemo	• CEA > 30 (ng/mL) • Tumor size > 40 (mm) • No. of chemotherapy cycles > 12 • Disease progression during first-line chemo

TSH two-stage hepatectomy, *ND* not done, *FLR* future liver remnant, *CEA* carcinoembryonic antigen, *PVE* portal vein embolization

maximum tumor size >40 mm and CEA at hepatectomy >30 ng/mL), and a predictive model for failure of TSH was developed based on logistic model [12]. For patients without any risk factor, the probability of failure was 10.5%. The addition of each subsequent factor increased the risk to 43.5%, 72.7%, and 88.5% for one, two, three and four factors, respectively. Based on this predictive model, we can assess the probability of failure of TSH before surgery. This model can contribute to a better selection of patients who will be submitted to TSH.

Short-Term Outcome

In our first report in 2000, we reported that the mortality rates were 0% and 15% after first-stage and second-stage hepatectomy, respectively, and postoperative complication rates were 31% and 45%, respectively [10]. Through the process of surgical development of TSH procedure, our recent update (2000–2012) revealed that 90-day mortality rates were 0.8% and 2.5% after first-stage and second-stage hepatectomy, respectively (P = 0.97), and postoperative complication (Clavien ≥ III [31]) rates were 14.4% and 33.3%, respectively (P = 0.0015) [12]. One patient died of acute myocardial infarction 10 days after first-stage hepatectomy, and two patients died of postoperative liver failure after major hepatectomy (≥3 segments) during second-stage. In the literature, postoperative complications after first-stage occurred in 0–37% of patients, and the postoperative mortality was 0–4%, respectively (Table 13.2). On the contrary, postoperative complications after second-stage occurred in 11–60% of patients, and the postoperative mortality was 0–6%, respectively (Table 13.3). Although the complications are obviously more frequently observed after second-stage than after first-stage, these morbidity/mortality rates are thought to be almost equivalent, compared to one-stage hepatectomy. These findings suggest that TSH procedure is no longer an experimental surgery and can be performed with acceptable morbidity/mortality rates.

Long-Term Outcome

Previously reported 5-year OS rate after completion of TSH ranged from 32 to 64%, with median survival time of 24–44 months [12, 13, 23, 26–29, 32–36]. In our recent updated data between 1992 and 2012, 1116 consecutive patients underwent initial hepatectomy for CLM at our institution. Among them, 139 patients (12.4%) were scheduled to undergo TSH for extensive CLM (six patients who underwent ALPPS were excluded). Of these, 46 patients (33.1%) could not proceed to the second-stage mainly because of disease progression after first-stage hepatectomy. On an intention-to treat (ITT) basis, the OS for patients who were scheduled to undergo TSH was significantly lower than that of those who underwent standard one-stage hepatectomy (5-year OS: 31.8 vs. 47.1%, median 38.4 vs. 55.2 months, P = 0.0004) (Fig. 13.4a). However, among the patients who underwent liver-curative surgery (liver R0 or R1), the OS for patients who complete TSH compared similarly with that of those who underwent standard one-stage hepatectomy (5-year OS: 41.3 vs. 48.0%, median 44.3 vs. 56.6 months, P = 0.40) (Fig. 13.4b). These findings suggest that if both sequential procedures of TSH are completed, comparable long-term survival with standard one-stage hepatectomy can be expected.

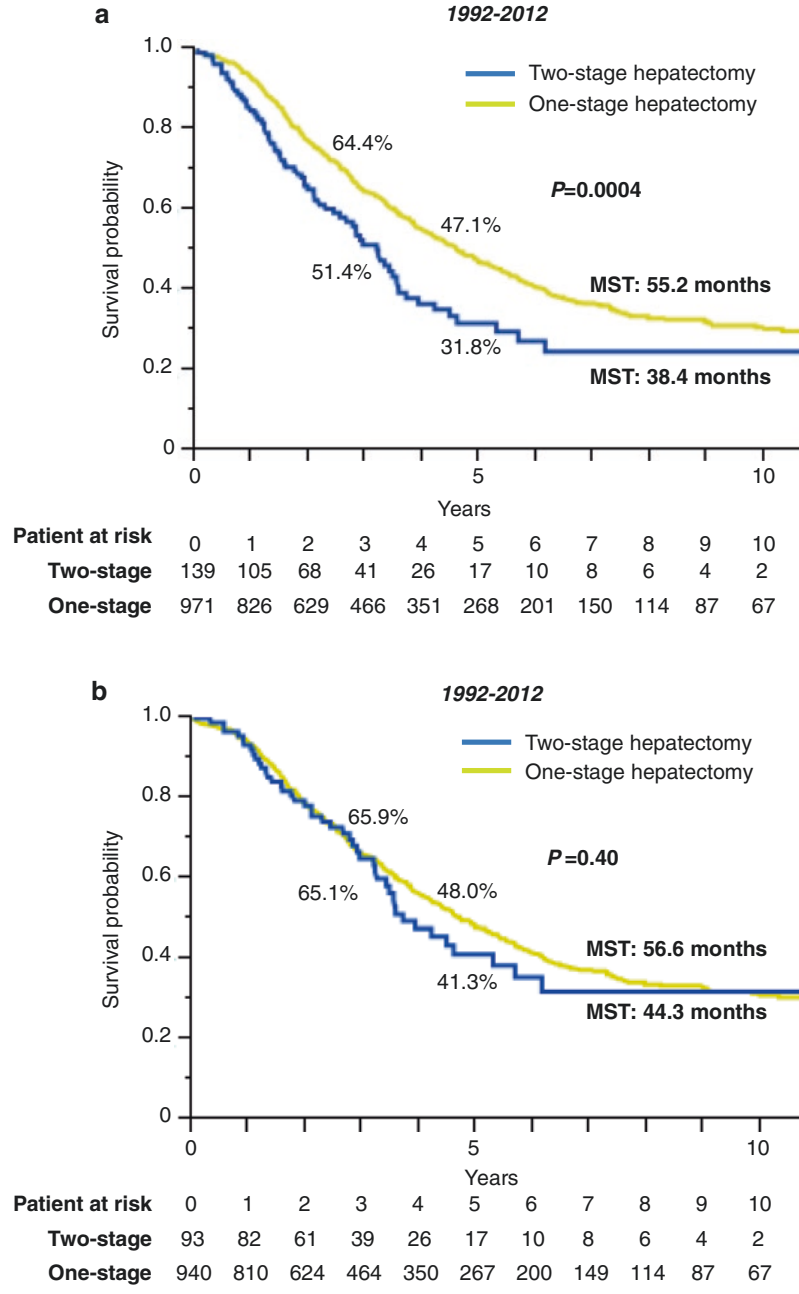

Fig. 13.4 (**a**) Overall survival for patients who were planned for two-stage hepatectomy ($n = 139$) and patients who underwent standard one-stage hepatectomy ($n = 971$), between 1992 and 2012 (intention-to-treat basis). (**b**) Overall survival for patients who completed two-stage hepatectomy ($n = 93$) and patients who underwent liver-curative one-stage hepatectomy ($n = 940$), between 1992 and 2012. *MST* mean survival time

Prognostic Factors of Survival After TSH

Previous studies reported several independent prognostic factors after TSH (Table 13.5). On an ITT basis (including the patients who failed to complete TSH), failure of TSH [30, 33] and major complications after first- or second-stage hepatectomy [33] were identified as independent prognostic factors of poor survival. On the contrary, among the patients who completed TSH, preoperative chemotherapy cycle ≥6 [27], tumor number ≥6 [13], presence of concomitant extrahepatic disease [13], and no postoperative chemotherapy

Table 13.5 Reported prognostic factors for survival after two-stage hepatectomy

Study	Year of publication	Country	No. of pts	5-year OS	Independent prognostic factors (multivariate)	Patients cohort
Wicherts et al.	2008	France	41	42	• Tumor number ≥ 6 • Concomitant extrahepatic disease • No postoperative chemotherapy	TSH completed cohort
Brouquet et al.	2011	USA	62	51	• Major complication after first- or second-stage • TSH failure	Whole cohort
Giuliante et al.	2014	Italy	102	32	• Chemotherapy cycle ≥ 6	TSH completed cohort
Failot et al.	2015	France	50	27 (3-year)	• TSH failure	Whole cohort

OS overall survival, *TSH* two-stage hepatectomy

[13] were reported as independent prognostic factors of poor survival after completion of TSH. The analyses of our data recently updated with the inclusion of 139 patients who were planned for TSH revealed that failure of TSH was the only independent prognostic factor in the whole cohort. Among the 93 patients who completed TSH, major complications (Clavien ≥ III) after second-stage and repeat surgery for recurrent disease were the independent prognostic factors of survival after TSH (unpublished data). It is obvious that the most important objective is to prevent the failure of TSH. In addition to that, however, keeping a low complication rate after second-stage (because complications after second-stage may lead to delay of postoperative chemotherapy or limitations of treatment options for recurrent disease) and aggressive repeat surgery for recurrence are thought to be crucial for long-term survival after TSH.

Future Perspective of TSH

Recently, associating liver partition and portal vein ligation for staged hepatectomy (ALPPS) has been reported as a novel form of TSH [37, 38]. ALPPS seems to offer two main advantages compared to 'conventional' TSH; rapid and higher volume increase of FLR and a shorter interval period between two procedures. As a result, the failure rate of ALPPS is almost 0 [39–44]. The higher feasibility of ALPPS may be able to overcome the drawback of "failure to complete two sequential procedures" in TSH. However, ALPPS is still in the process of evolution and the oncological outcome is still uncertain. For the treatment of extensive multiple bilobar CLM, it could be essential that the indications of TSH and ALPPS should be determined by considering the advantage and disadvantage of each procedure as well as their long term outcome.

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