Percutaneous hepatic perfusion in unresectable liver metastases: focus on ocular melanoma

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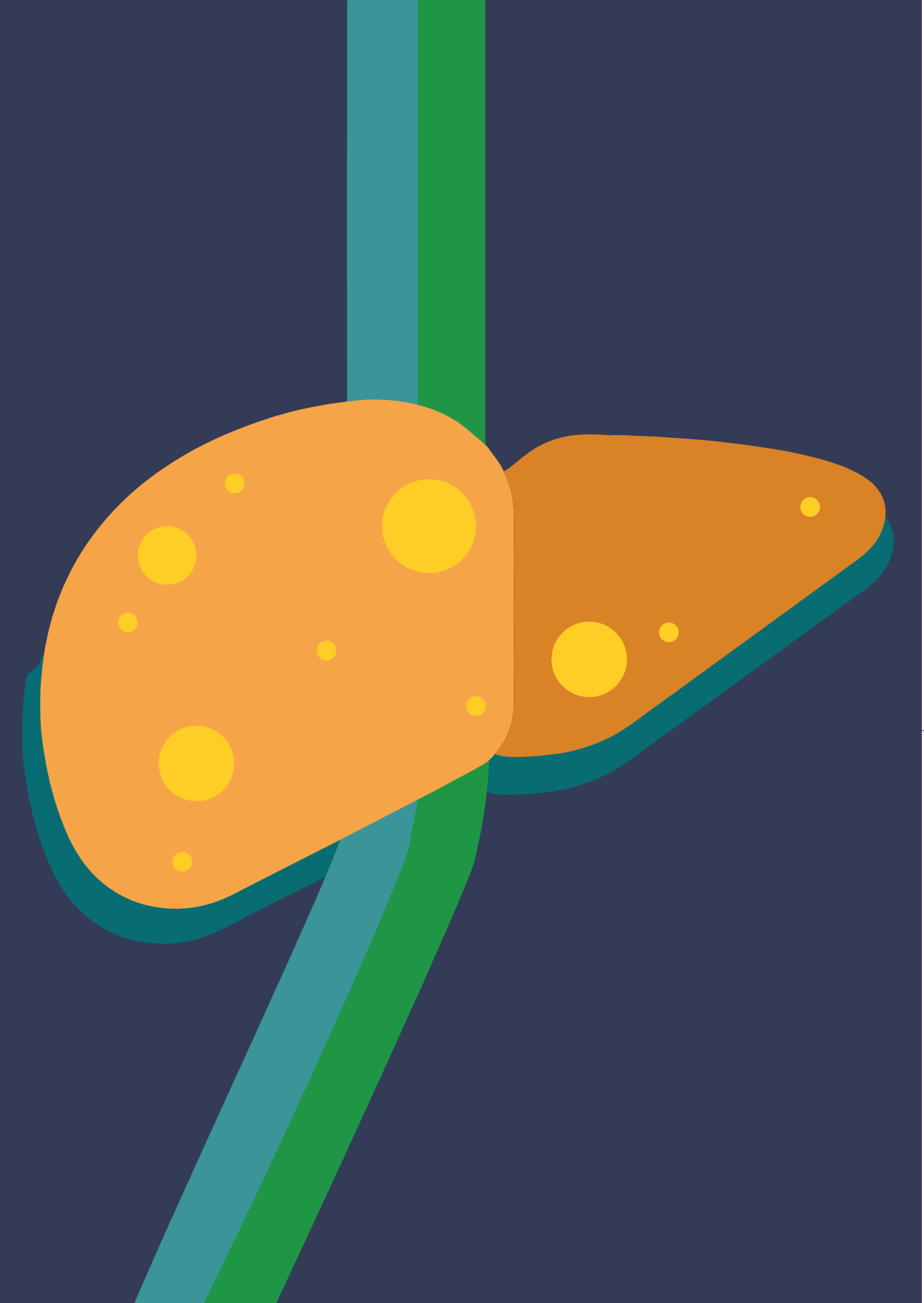

CHAPTER 4

Embolization of variant hepatic arteries in patients undergoing percutaneous hepatic perfusion for unresectable liver metastases from ocular melanoma

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ABSTRACT

Purpose

In patients undergoing percutaneous liver perfusion with melphalan (M-PHP), the presence of variant hepatic arteries (HAs) may require catheter repositioning and thus prolong procedure time. Coil-embolization of variant HAs may enable M-PHP with a single catheter position as occlusion of variant HAs results in redistribution of flow through preexisting intrahepatic arterial collaterals. Aim of this study was to evaluate whether redistribution of flow has any negative effect on therapeutic response in ocular melanoma patients undergoing M-PHP.

Methods

We retrospectively analyzed pretreatment angiograms in all 32 patients that underwent M-PHP between January 2014 and March 2017 for unresectable liver metastases from ocular melanoma. Patients that underwent embolization of a variant left HA (LHA) or middle HA (MHA) during pretreatment angiography followed by at least one technically successful M-PHP, were included for further analysis. Redistribution of arterial flow was evaluated on angiography and cone-beam CT (CBCT) images. In each patient, tumor response in liver segments with redistributed blood flow was evaluated using RECIST 1.1 and mRECIST, and then compared to tumor response in segments without flow redistribution. Follow-up scans were reviewed to evaluate progression of liver metastases.

Results

A total of 12 patients were included. Replaced LHA embolization resulted in redistribution of flow to segment(s) 2 (*n* = 3), 2 and 3 (*n* = 5), and 2, 3 and 4 (*n* = 2). MHA embolization resulted in redistribution of flow to segment 4 (*n* = 2). Successful redistribution was confirmed by angiography and/or CBCT in all patients. Tumor response was similar for redistributed and non-redistributed liver segments in 8 out of 9 patients (89%) according to RECIST 1.1, and in 7 out of 8 patients (88%) according to mRECIST. In three patients, tumor response was not evaluable according to RECIST 1.1 or mRECIST as metastases were too small to be categorized as target lesions (*n* = 1), or target lesions were confined to non-redistributed segments (*n* = 2). In one patient, tumor response was not evaluable according to mRECIST as target lesions in the redistributed segments were hypovascular. After a median follow-up time of 17.1 months (range 9.1-38.5), hepatic progression was seen in 9 out of 12 patients with a median time to progression of 9.9 months (range 2.5-17.7). Progression of liver metastases was never seen in the redistributed liver segments only.

Conclusion

Flow redistribution in liver segments by coil-embolization of variant HAs is a feasible technique that does not seem to compromise tumor response in patients undergoing M-PHP.

INTRODUCTION

Percutaneous isolated hepatic perfusion with melphalan (M-PHP) is a minimally invasive and repeatable technique for the treatment of malignant liver tumors. The superiority of M-PHP over standard available therapy has been demonstrated in a randomized controlled multicenter phase III trial for patients with liver metastases from cutaneous and ocular melanoma.[1] In the Netherlands, M-PHP is now regarded as first line therapy in patients with liver metastases from ocular melanoma as such patients often present with unresectable metastases confined to the liver and effective systemic therapies are not available.[2-4]

A common complication of M-PHP is bone marrow suppression resulting in anemia, thrombocytopenia, and/or neutropenia. This is caused by the inability of hemofiltration cartridges to extract all melphalan allowing a limited amount of chemotherapeutics to reach the systemic circulation.[5,6] In an attempt to reduce bone marrow suppression, a new second-generation filter (GEN 2 filter) was developed by Delcath Systems (Delcath Systems, New York, NY, USA). Although the mean filter extraction rate of the GEN 2 filter is indeed higher compared to first-generation filters (86% *vs.* 77%), severe hematologic toxicity is still reported in patients that underwent M-PHP using the GEN 2 filter.[5-7] Additionally, it was demonstrated that the extraction rate of the GEN 2 filter decreases over time, probably due to saturation of the filter.[6] This means that patients with a prolonged extracorporeal filtration time may be at risk of increased systemic exposure to melphalan. Furthermore, a longer extracorporeal filtration time results in a prolonged cardiac strain, an increased risk of hemolysis and hypothermia. Therefore, extracorporeal filtration time should be limited when possible.

Prolonged extracorporeal filtration time can result from the presence of variant hepatic arterial anatomy as repositioning of the infusion catheter may be required to deliver chemotherapy to all liver metastases. We address this problem by using so-called 'redistribution of flow' in which variant hepatic arteries (HAs) are embolized with coils, after which perfusion of liver segments is taken over by preexisting intrahepatic arterial collaterals originating from an adjacent segment. This technique is well studied in patients with liver tumors treated with radioembolization[8-11] and hepatic arterial infusion chemotherapy.[12-16] Two studies on yttrium-90 (^{90}Y) radioembolization found a similar tumor response for both redistributed and non-distributed segments in 92-96% of patients.[9,11] Although it is also a well-established technique in hepatic arterial infusion chemotherapy, concern has been raised by some that redistribution of flow may have an unfavorable effect on tumor response.[17,18] The effect of flow redistribution on therapeutic response of liver metastases treated with M-PHP needs further investigation.

We hypothesized that flow redistribution in the liver by coil-embolization of variant HAs prior to M-PHP has no adverse effect on therapeutic response in patients with liver metastases from ocular melanoma. In order to demonstrate this, we retrospectively reviewed our patient series.

METHODS

Study design and population

In this retrospective study, we reviewed pretreatment angiograms in all 32 patients that underwent M-PHP between January 2014 and March 2017 as a treatment of unresectable liver metastases from ocular melanoma. Of these 32 patients, 20 were excluded and 12 patients (median age, 62 years; age range, 44-71) were found eligible for further analysis in this study. Exclusion criteria were the absence of an embolized variant HA (*n* = 18) and no technically successful M-PHP (*n* = 2), due to cardiac ischemia and heparin-induced thrombocytopenia.

All patients received their treatment as part of a prospective phase II trial, and therefore had given their informed consent. Approval was obtained from the local medical ethics committee.

Pretreatment angiography and M-PHP

Prior to M-PHP, all patients underwent selective angiography of the celiac trunk in order to determine the hepatic arterial circulation and formulate the best strategy for infusion of melphalan. Catheterization was performed using a 5F catheter (Radifocus® angiographic catheter general-visceral cobra, Terumo, Tokyo, Japan or Cordis® angiographic catheter C2, Cordis Corporation, Miami Lakes, FL, USA) with a 2.4F or 2.7F Progreat (Terumo, Tokyo, Japan) microcatheter. If deemed necessary, hepatico-enteric anastomoses such as the gastroduodenal or right gastric artery, were embolized to prevent inadvertent leakage of melphalan during M-PHP. Occlusion of replaced left HAs (LHAs) or middle HAs (MHAs) was performed if; 1) perfusion of the entire liver was not feasible using a single infusion site, and 2) repositioning of the catheter was considered challenging and/ or time-consuming. Embolization was performed with 2 to 8 mm detachable coils (Interlock; Boston Scientific, Marlborough, MA, USA). Angiography was performed using a Philips AlluraClarity Interventional X-ray System with Clarity IQ technology (Philips Medical Systems, Best, The Netherlands). Performance of C-arm cone-beam CT (CBCT) to ensure enhancement of the entire liver and exclude vascular tumor supply from extrahepatic collaterals was left to the discretion of the interventional radiologist. CBCT images were acquired during a 10 seconds rotation of the Philips AlluraClarity C-arm (300 images, 240° arc). Tube voltage was 120 kV, tube current was automatically adjusted to each patient by the system (range 50-325 mA). Contrast medium (Iohexol, 300 mg iodine/ml, Omnipaque 300, GE Healthcare, Shanghai, China) was injected with a flow rate of 1-2 ml/sec for lobar injections and 2-3 ml/sec for injections from the proper or common hepatic artery. The injected contrast volume was calculated using the equation ´volume = (scan delay + scan time) x flow rate´ with the scan delay being the time between the start of injection and tumor enhancement at angiography.

Initial M-PHPs were performed approximately one week after angiography. Details of the procedure were described elsewhere.[19] As per protocol, most patients underwent two

cycles of M-PHP at a 6-9 weeks interval with 3 mg melphalan/kg and maximum dose of 220 mg. No CBCT was performed at the time of the actual M-PHP treatment.

Imaging, image interpretation and evaluation of response

Pretreatment angiograms were studied and types of embolized variant HAs were recorded. Whether the embolization resulted in successful redistribution of flow was evaluated on angiography and CBCT. Successful redistribution was defined as enhancement of all segmental HAs on angiography and enhancement of all liver segments on CBCT.

All patients underwent a contrast-enhanced CT of chest and abdomen (arterial and portovenous phase) 5-10 weeks after the first and second M-PHP. After this, follow-up contrast-enhanced CT was performed every three months. An additional MRI of the liver was performed in patients with lesions that were difficult to visualize on contrast-enhanced CT.

Tumor response was evaluated according to Response Evalution Criteria in Solid Tumors 1.1 (RECIST 1.1) and modified RECIST (mRECIST). In each patient, the response of target lesions previously supplied by a variant HA and now depending on intrahepatic arterial collaterals, was compared with the response of target lesions in segments not depending on collaterals (Figure 1). Retrospective consensus reading of scans was performed by two readers. A maximum of two target lesions were selected in both liver segment(s) with flow redistribution and non-redistributed segments (i.e. a maximum of four target lesions per liver). A maximum of two target lesions was chosen in order to have; 1) a scoring system similar to RECIST 1.1. and mRECIST, 2) consistent response evaluation in different patients (the number of lesions varied considerably between patients), 3) consistent response evaluation between segments with and without flow redistribution (in most cases more lesions in segments without flow redistribution), and 4) for practical reasons (most patients presented with numerous lesions).

Lesions were considered as target lesions if their longest diameter was ≥ 10 mm and borders were defined well enough to allow reliable measurement.

Scans performed during further follow-up were reviewed to evaluate progression of liver metastases. In case of hepatic progression, we determined whether progression (i.e. growth of existing lesions or new lesions) occurred in the redistributed or non-redistributed liver segments.

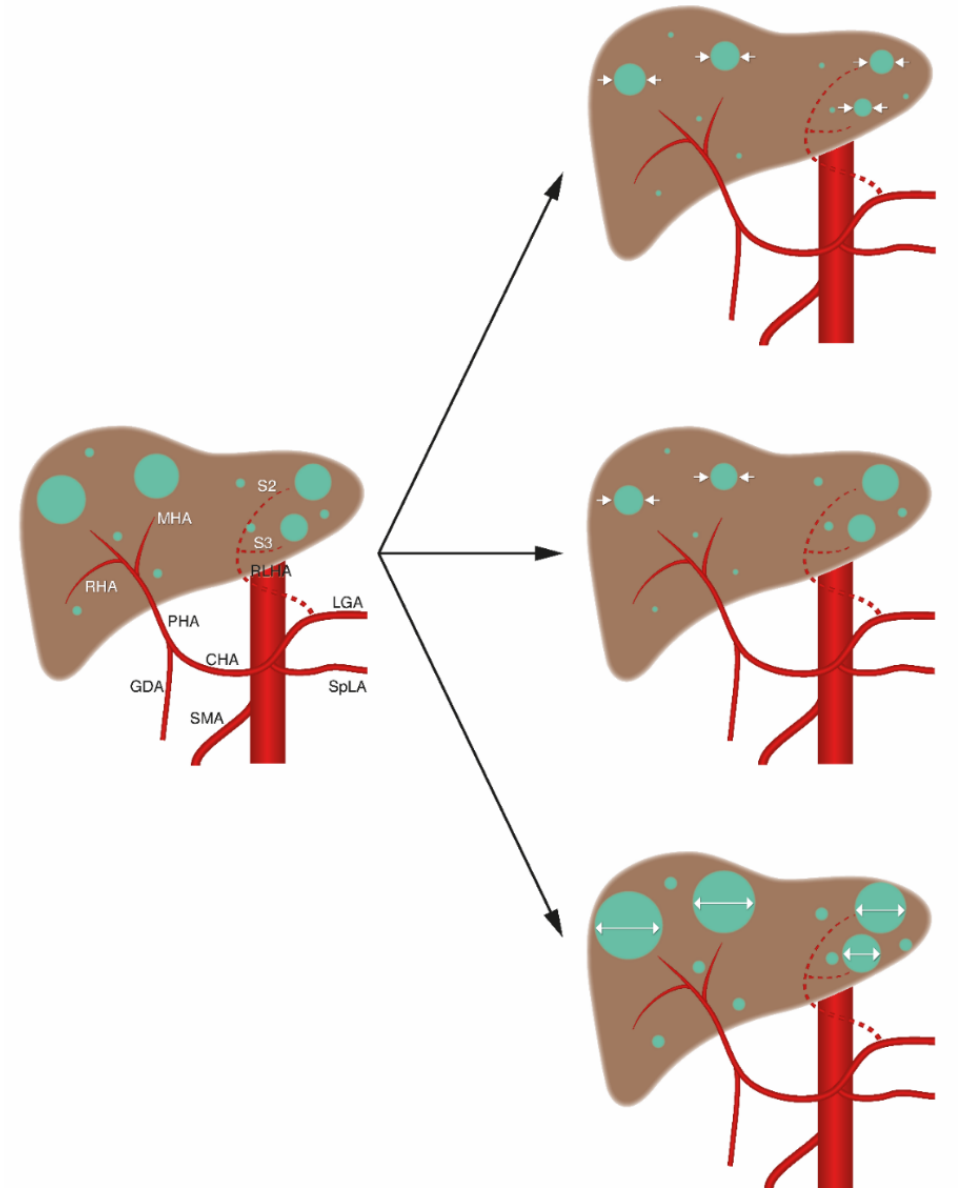

FIGURE 1. Assessment of the effect of flow redistribution on therapeutic response of liver metastases is schematically depicted in this liver in which a variant LHA is embolized (dotted)
If all tumors responded positively (top), redistribution seemed to have no negative effect. If tumors in non-redistributed segments responded positively but tumors in redistributed segments showed no therapeutic response (middle), we interpreted this as evidence that redistribution had a negative effect. If all tumors uniformly progressed (bottom), the effect of redistribution would not be evaluable because even lesions in the non-redistributed segments showed no therapeutic response which would suggest therapy resistance.
CHA common hepatic artery, *GDA* gastroduodenal artery, *LGA* left gastric artery, *LHA* left hepatic artery, *MHA* middle hepatic artery, *PHA* proper hepatic artery, *RHA* right hepatic artery, *RLHA* replaced left hepatic artery, *SMA* superior mesenteric artery, *SplA* splenic artery, *S* segment.

RESULTS

All patients had bilobar multifocal disease and underwent a median of two M-PHP cycles (range, 1-4). Patient demographics and metastatic details are summarized in Table 1.

Replaced LHA embolization was performed in 10 out of 12 patients, leading to redistribution of flow in liver segment 2 (*n* = 3), segments 2 and 3 (*n* = 5), or segments 2, 3 and 4 (*n* = 2). Two patients underwent embolization of a segment 4 artery. Figure 2 shows schematic diagrams of various types of variant HAs that were embolized.

TABLE 1. Demographic data and metastatic details in patients with an embolized HA and ≥ one technically successful M-PHP (*n* = 12)

Parameters	
Gender [n (%)]	
Men	5 (41.7)
Women	7 (58.3)
Age at first M-PHP [years; median (range)]	62 (44-71)
BMI [kg/m^2; median (range)]	26.9 (20.4-32.3)
Type of metastases [n (%)]	
Synchronous	3 (25.0)
Metachronous	9 (75.0)
Mutations in liver metastases	
GNA11	5 (41.7)
GNAQ	7 (58.3)
Radiological aspect metastases [n (%)]	
Hypovascular	1 (8.3)
Hypervascular	9 (75.0)
Mixed	2 (16.7)
Number of metastases [n (%)]	
6-9	2 (16.7)
≥ 10	10 (83.3)
Number of M-PHP treatments	
1	1 (8.3)
2	9 (75.0)
3	1 (8.3)
4	1 (8.3)
Prior therapy for liver metastases [n (%)]	
Systemic therapy[a]	2 (16.7)
Regional therapy[b]	1 (8.3)
Regional and systemic therapy	1 (8.3)
No prior therapy	8 (66.7)
Follow-up [months; median (range)]	17.1 (9.1-38.5)

[a] Randomized phase II SUMIT-trial (Selumetinib with Dacarbazin vs. placebo), ipilimumab, phase I AEB071-study (Protein Kinase C Inhibitor), dendritic cell therapy.
[b] Radiofrequent ablation and/or metastasectomy.
BMI body mass index, *M-PHP* percutaneous hepatic perfusion with melphalan.

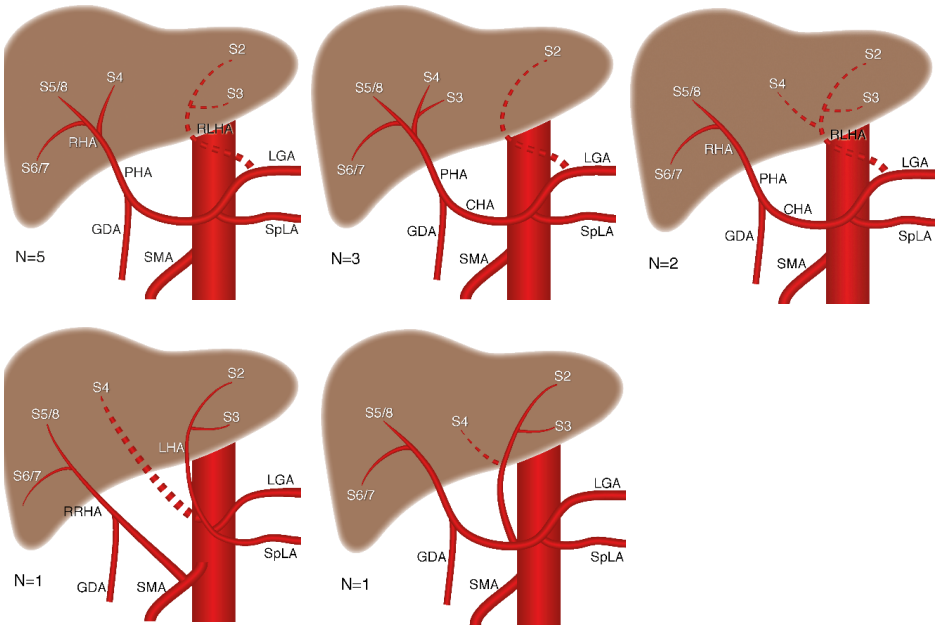

FIGURE 2. Schematic drawings of redistribution of flow in various liver segments in all patients after embolization of a variant LHA (*n* = 10, a-c) or MHA, i.e. S4 artery with proximal origin (*n* = 2, d and e)
CHA common hepatic artery, *GDA* gastroduodenal artery, *LGA* left gastric artery, *LHA* left hepatic artery, *MHA* middle hepatic artery, *PHA* proper hepatic artery, *RHA* right hepatic artery, *RLHA* replaced left hepatic artery, *SMA* superior mesenteric artery, *SplA* splenic artery, *S* segment.

Post-embolization angiography showed successful redistribution of flow in all patients (Figure 3). This was confirmed by CBCT in 9 out of 12 patients. CBCT images were not available for two patients (no. 3 and 11), and in one patient (no. 7) CBCT showed no enhancement in the redistributed segments. This was probably due to the scanning delay being too short which resulted in acquisition of the images prior to contrast medium arrival.

Tumor response in both redistributed and non-redistributed liver segments was not evaluable according to RECIST 1.1 and mRECIST in 3 out of 12 patients (Table 2). Reasons were the absence of target lesions with all metastases measuring < 10 mm (*n* = 1), and target-lesions only observed in non-redistributed segments (*n* = 2). In one patient, tumor response was not evaluable according to mRECIST because not all target lesions were hypervascular.

Target tumor response in redistributed and non-redistributed liver segments was evaluable according to RECIST 1.1 and mRECIST in 9 out of 12 patients (Table 2, Figure 4). According to RECIST 1.1, partial response was seen in both redistributed and non-redistributed liver segments in 8 out of 9 patients (89%). A discrepancy in radiological response was seen in one patient: partial responnse in the redistributed liver segment compared to stable disease) in non-redistributed liver segments. According to mRECIST, a similar tumor response

in redistributed and non-redistributed segments was observed in 7 out of 8 patients (88%). Complete response and progressive disease were seen in 5 and 2 patients, respectively. A discrepancy in radiologic response was seen in one patient: complete response in the redistributed liver segment compared with partial disease in non-redistributed liver segments.

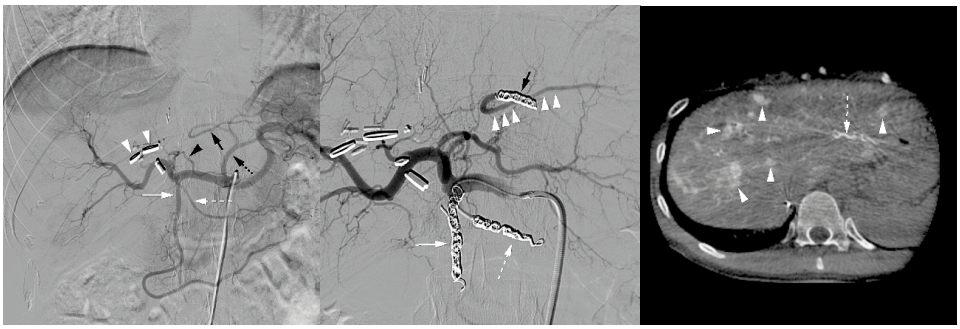

FIGURE 3. Hepatic vascular mapping and coil-embolization prior to M-PHP in a 44-year-old female with bilateral liver metastases from ocular melanoma

Angiographic images from the celiac trunk (a) show the gastroduodenal artery (GDA) (white arrow), right gastric artery (RGA) (dotted white arrow), a segment 3 artery (black arrowhead) originating from the left hepatic artery (LHA) and a segment 2 (S2) artery (black arrow) originating from the left gastric artery (dotted black arrow). Surgical clips after prior metastasectomy are seen (white arrow heads). After coil embolization of the GDA (white arrow), RGA (dotted white arrow) and S2 artery (black arrow) (b), redistribution of flow (white arrowheads) to S2 was accomplished. Cone-beam CT confirms redistribution of flow (c, dotted white arrow) and shows multiple hypervascular metastases in both liver lobes (white arrowheads).

TABLE 2. Tumor response in redistributed and non-redistributed segments

			No. of metastases			Response in redistributed *vs.* non-redistributed segments	
Pt number	Redistributed segment(s)	Aspect of metastases	Total	Redistributed segment(s)	Non-redistributed segments	According to RECIST 1.1	According to mRECIST
1	2	Hyper	≥ 10	2-5	≥ 10	PR *vs.* PR	CR *vs.* CR
2	2, 3	Hypo	≥ 10	≥ 10[a]	≥ 10[a]	N/A	N/A
3	2, 3, 4	Hyper	≥ 10	2-5	≥ 10	PR *vs.* PR	PR *vs.* PR
4	2, 3	Hyper	6-9	2-5	2-5	PR *vs.* PR	CR *vs.* CR
5	4	Hyper	≥ 10	1	≥ 10	PR *vs.* PR	CR *vs.* CR
6	2	Hyper	≥ 10	≥ 10	≥ 10	PR *vs.* SD	CR *vs.* CR
7	2, 3	Hyper	≥ 10	0	≥ 10	N/A	N/A
8	2, 3	Mixed[b]	≥ 10	2-5	≥ 10	PR *vs.* PR	CR *vs.* CR
9	2	Hyper	≥ 10	2-5	≥ 10	PR *vs.* PR	CR *vs.* PR
10	4	Hyper	≥ 10	2-5	≥ 10	PR *vs.* PR	PR *vs.* PR
11	2, 3, 4	Hyper	≥ 10	2-5[a]	6-9	N/A	N/A
12	2, 3	Mixed[c]	6-9	2-5	6-9	PR *vs.* PR	N/A

[a] No target lesions defined because of small size (all < 1 cm).
[b] Target lesions in redistributed and non-redistributed segments were hypervascular.
[c] Only 1 out of 4 target lesions was hypervascular.
Hyper hypervascular, *Hypo* Hypovascular, *RECIST 1.1* Response Evaluation Criteria in Solid Tumors 1.1, *mRECIST* modified RECIST, *PR* partial response, *CR* complete response, *SD* stable disease, N/A not available.

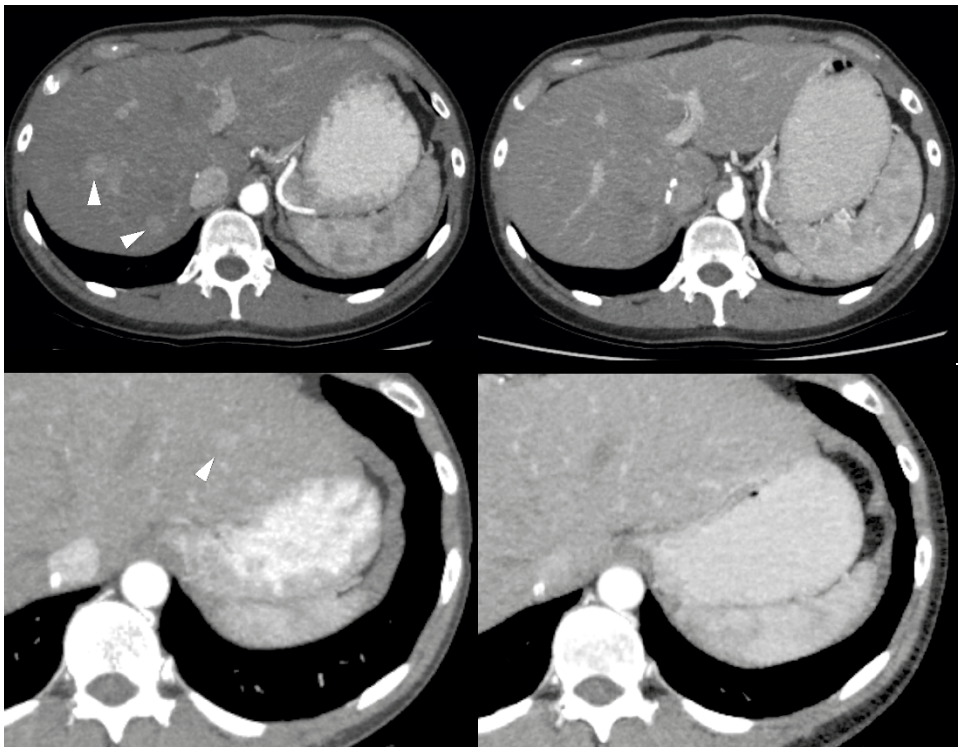

FIGURE 4. a-d. Tumor response in non-redistributed (a, b) and redistributed (c, d) liver segments after two cycles of M-PHP, in a 44-year-old female with bilateral liver metastases from ocular melanoma
Pretreatment CT in arterial phase shows two hypervascular metastases in the right liver lobe (white arrowheads) (a), and one hypervascular metastasis in segment 2 (S2, white arrowhead) (c). CT after two cycles of M-PHP shows complete disappearance of contrast enhancement in the metastases in the right liver lobe (b), and S2 (d). This is compatible with a complete response according to mRECIST in the non-redistributed and redistributed liver segments. Posttreatment CT in portovenous phase (not shown) showed all metastases as hypodense lesions with a decrease in size after treatment, compatible with partial response according to RECIST 1.1 in the non-redistributed and redistributed liver segments.

Three out of 12 patients (no. 2, 3 and 10) received an MRI prior to treatment and at follow-up imaging as their liver lesions were not well visualized on contrast-enhanced CT. In the other 9 patients, contrast-enhanced CT was sufficient to image liver lesions and evaluate tumor response. Seven out of 12 patient (no. 3-7, 11 and 12) underwent an additional (18) F-fluorodeoxyglucose-positron emission tomography combined with unenhanced CT (FDG-PET/CT) at some point during follow-up. The median time period between first M-PHP and the performance of the FDG-PET/CT was 7.8 months (range, 4.0-37.3).

After a median follow-up time of 17.1 months (range, 9.1-38.5), progression of liver metastases was seen in 9 out of 12 patients with a median time to progression of 9.9 months (range, 2.5-17.7). Progression was seen in liver segments without flow redistribution only (n = 5) or in both redistributed and non-redistributed segments (n = 4) (Table 3).

TABLE 3. Hepatic progression in redistributed and non-redistributed segments

Pt number	Hepatic progression (Y/N)	TTHP (months)	Progression in redistributed segment(s) (Y/N)	Progression in non-redistributed segments (Y/N)	FU (months)	Status
1	Y	2.5	N	Y	38.5	Dead
2	Y	9.7	Y	Y	37.9	Alive
3	N	N/A	N/A	N/A	35.6	Alive
4	Y	17.7	N	Y	32.9	Alive
5	Y	15.0	N	Y	29.6	Dead
6	N	N/A	N/A	N/A	9.1	Dead
7	Y	10.9	N	Y	17.4	Dead
8	Y	6.3	N	Y	15.8	Dead
9	Y	9.9	Y	Y	16.5	Dead
10	Y	11.2	Y	Y	16.8	Alive
11	Y	6.8	Y	Y	16.3	Alive
12	N	N/A	N/A	N/A	13.1	Alive

TTHP time to hepatic progression, *FU* follow-up, *N/A* not available.

DISCUSSION

This study shows that in patients with liver metastases from ocular melanoma treated with M-PHP, tumor response in liver segments with redistributed arterial flow is not compromised compared with tumor response in non-redistributed liver segments. This implies that coil-embolization of replaced LHAs or MHAs in order to simplify the administration of melphalan has no adverse effect on therapeutic response in these patients. Coil-embolization of replaced right HAs was not performed as in all cases they were considered as the dominant artery to supply the liver. We found it was uncertain whether whole liver perfusion through the LHA would be sufficient and not compromise tumor response.

Approximately 40% of all ocular melanoma patients will develop metastases within 10 years after diagnosis of the primary tumor.[20] Liver metastases occur in 93-95% of patients with metastatic ocular melanoma, often affecting both liver lobes.[20-22] Effective systemic therapies are lacking and therefore patients with liver-dominant disease should be considered for liver-directed therapies such as transarterial (chemo-)embolization, radioembolization and isolated hepatic perfusion (IHP). M-PHP is a novel minimally invasive and repeatable alternative to IHP and is performed more and more in these patients.[1,23-28] In a recently conducted randomized controlled multicenter phase III trial, treatment with M-PHP was compared with best available care in patients with liver metastases from ocular melanoma.[1] It was demonstrated that M-PHP significantly prolongs both hepatic progression free survival (7.0 *vs*. 1.6 months) and overall progression free survival (5.4 *vs*. 1.6 months).

Redistribution of arterial flow has been well established in patients with liver tumors treated with ^{90}Y radioembolization and is used to limit the number of administration sites,

improve selectivity of treatment, and reduce the risk of non-target radioembolization.[9-11,29] Studies on patients undergoing radioembolization demonstrated that coil-embolization led to successful flow redistribution in 89-95.8% prior to therapy, as depicted by technetium-99m-labeled macroaggregated albumin (99mTc-MAA) scintigraphy, angiography and/or CBCT.[11,21,23] In two studies, tumor response in redistributed and non-redistributed liver segments were compared after ^{90}Y radioembolization. The first study found a similar tumor response in 22 out of 24 patients (92%), and the other study found a uniform partial response and stable disease in 21 out of 22 patients (96%).[9,11] However, these results may not be applicable to M-PHP.

Unlike chemotherapy used in M-PHP, microspheres have a moderate embolic effect that may cause alteration of flow during infusion. There may be preferential flow of microspheres to certain liver segments at the beginning of the infusion, but blockage of the end-arterioles of these segments by microspheres may cause subsequent preferred flow to other areas. Coil-embolization to establish redistribution of flow is also common practice in patients undergoing hepatic arterial infusion chemotherapy, although there have been concerns that this might have an adverse effect on tumor response.[17,18] Results of redistribution of flow in hepatic arterial infusion chemotherapy may also not be applicable to M-PHP. In M-PHP, a double balloon catheter is used to isolate the hepatic veins from the systemic circulation and this may cause alterations in flow patterns and even obstruction of the left and/or middle hepatic vein. Furthermore, systemic blood pressure during M-PHP is lowered due to a reduced cardiac preload. These hemodynamic changes may have a negative impact on tumor response in liver segments with redistributed flow. We therefore conducted the present study.

In our study, both RECIST 1.1 and mRECIST criteria were used for evaluating tumor response. International guidelines support the use of mRECIST for radiological tumor response in patients with hepatocellular carcinoma as this may predict survival outcome better than RECIST 1.1.[30,31] And although shown to be suitable for tumor response in other malignancies such as intrahepatic cholangiocarcinoma[32], mRECIST has not been validated for ocular melanoma. In our study, we found anecdotal evidence that mRECIST may be superior to RECIST 1.1 in assessing response of ocular melanoma liver metastases to treatment with M-PHP. In one patient, we noticed complete devascularization of lesions in both redistributed and non-redistributed liver segments, which correlates with complete response according to mRECIST. According to RECIST 1.1, however, the liver segment with flow redistribution showed PR, but the non-redistributed segments showed stable disease (sum of dimension of target lesions decreased with 21%). An additional FDG-PET/CT, performed because of suspected bone metastases, showed no FDG uptake in the liver. Since FDG uptake in the bone metastases was seen, viable liver metastases were unlikely, confirming complete response.

Our study has several limitations. First of all, the number of patients was small. Further studies are needed to validate our conclusions. Nevertheless, our study provides a first

indication that coil-embolization of variant HAs may be a useful and safe strategy to limit extracorporeal filtration time in M-PHP. Second, we assumed that performing redistribution of flow limits the infusion time of melphalan during M-PHP. In our study, the mean total extracorporeal filtration time was 83 min (range, 60-95). However, we could not compare this with a group of patients with variant HAs that underwent M-PHP without redistribution of flow. Although we can therefore not substantiate that flow redistribution will result in shorter extracorporeal filtration time, this seems highly plausible.

In conclusion, flow redistribution in liver segments by coil-embolization of replaced LHAs or MHAs does not seem to affect tumor response of metastases from ocular melanoma treated with M-PHP. Redistribution of flow is a feasible technique that might shorten extracorporeal filtration time in patients with a replaced LHA or MHA without compromising tumor response. Larger studies are needed to confirm our conclusions. Studies are also needed to evaluate whether coil-embolization of replaced RHAs may also be feasible without compromising tumor response.

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