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Mohamed Nabil
Tatjana Gruber
Danny Yakoub
Hanns Ackermann
Stephan Zangos
Thomas J. Vogl

Repetitive transarterial chemoembolization (TACE) of liver metastases from renal cell carcinoma: Local control and survival results

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M. Nabil · T. Gruber · S. Zangos · T. J. Vogl
Institute of Diagnostic and Interventional Radiology, Johann Wolfgang Goethe University, Frankfurt am Main, Germany

D. Yakoub
Department of Biosurgery and Surgical Technology, Imperial College London, St Mary's Hospital, London, UK

H. Ackermann
Department of Biostatistics and Medical Information, Johann Wolfgang Goethe University, Frankfurt am Main, Germany

M. Nabil (✉)
Institut für Diagnostische und Interventionelle Radiologie, Klinikum der Johann Wolfgang Goethe-Universität,
Theodor-Stern-Kai 7,
60590 Frankfurt am Main, Germany
e-mail: sh7aber@yahoo.com
Tel.: +49-69-63017271
Fax: +49-69-63015252

Abstract The purpose was to evaluate the effectiveness of transarterial chemoembolization (TACE) in local tumor control and survival in patients with hepatic metastases from renal cell carcinoma (RCC). Prospective evaluation of TACE treatment outcome in 22 patients recruited from 1999 and 2005 was performed. The chemotherapeutic agent used was mitomycin only in 45% of the patients and mitomycin together with gemcitabine in the other 55%. The embolizing materials used in all of the patients were iodized oil (lipiodol) and degradable starch microspheres. Local response was evaluated by MRI and judged according to Response Evaluation Criteria in Solid Tumors (RECIST). Mean and median survival and survival probability after diagnosis and treatment were both calculated by Kaplan-Meier method. Partial response was achieved in 13.7%, stable disease in 59% and progressive disease in 27.3% of patients. Survival time from the diagnosis of metastases ranged from 18 to 307 months and from 2.2 to 35 months from the start of TACE treatment. The median and mean survival times from the date of diagnosis were 68.6 and 102.9 months, respectively. The median and mean survival times from the start of TACE were 8.2 and 11.7 months, respectively. Survival probability from the start of treatment was 31% after 1 year and 6% after 2 years. TACE can result in a favorable local tumor response in patients with hepatic metastases from RCC, but survival results are still limited.

Keywords Renal · Carcinoma · Liver · Metastases · Chemoembolization · TACE

Introduction

Transarterial chemoembolization (TACE) has been established as a palliative, symptomatic and neoadjuvant modality in the management of hepatocellular carcinoma. It was performed for similar indications in cases of liver metastases. Many centers that advocate this treatment measure in liver metastases patients have repeatedly presented satisfactory results. Among the primary tumors causing liver metastases, digestive system malignancies, especially colorectal carcinoma, are the most common. TACE was successfully applied in patients with liver metastases from colorectal carcinoma [1–5], gastric carcinoma [6, 7], neuroendocrine malignant tumors [8–12], malignant melanoma [13, 14] and breast carcinoma [15].

Renal cell carcinoma is one of the relatively less common tumors causing liver metastases, and this might explain the lack of publications dedicated to this category of patients treated by TACE. Theses metastases are characterized by their hypervascularity, which makes chemoembolization more feasible and effective. We present here our data for patients with hepatic metastases from renal cell carcinoma treated by TACE in our institution to evaluate its role in local tumor control and its survival benefit.

Materials and methods

In a prospective study, a total of 22 patients (13 males and 11 females) were treated in our institute using TACE for liver metastases from renal cell carcinoma. The study protocol was approved by our ethics committee, and informed consent was obtained from all patients prior to treatment. The age range of included patients was 36 to 79 years (mean age, 63.7 years). In all patients, the primary tumor had been resected, and systemic chemotherapy had been applied prior to the TACE course. The number of TACE sessions ranged from 3 to 17 (mean=6.1). Eighteen of the included patients suffered from extrahepatic metastases. Therefore, TACE was not performed with a curative intention. This principle was clearly explained to all of the patients before receiving their consent. The indication for TACE was rather palliative in all our patients to reduce the tumor load in the liver and maintain the best possible liver function. In each patient, the sum of volumes of all the lesions and the liver volume were calculated to estimate the liver tumor load. Only patients with less than 70% tumor load were included. The involvement pattern was bilobar in 14 patients, right lobar only in 6 patients and left lobar only in 2 patients. The tumor load was 50 to 70% in 11 patients, all of whom had bilobar involment, and 25 to 50% in 7 patients. The remaining four patients had a tumor load less than 25%.

In eight patients TACE was performed for symptomatic indications, which were pressure on biliary tracts in three patients, diaphragmatic involvement in one patient, in addition to pain due to capsular invasion in six patients. Exclusion criteria approved by our institutional review board were tumor involvement of more than 70% of the liver volume, because in this case the treatment might compromise the liver function, and patients with locally irresectable primary tumor.

TACE technique

All the TACE procedures were performed by the same radiologist (T.V.), who has more than 15 years' experience in interventional radiology. Hepatic catheterization was performed using a 4–5 F Cobra catheter advanced into the hepatic artery proper distal to the gastroduodenal and right gastric artery origins. Depending on the size, location and the arterial supply to the tumor, the tip of the catheter was advanced further into segmental arteries. When the selective or super-selective catheterization was problematic, a Turbo-Tracker or Renegade 3F microcatheter (Boston Scientific, Galway, Ireland) was used. The chemotherapeutic agents used were a maximum of 10 mg/m2 mitomycin C (Medac, Hamburg, Germany) alone in 10 (45%) of the patients or in combination with 1,000–2,000 mg Gemcitabine (Gemzar®,Eli Lilly and Company, Indianapolis, IN) in 12 (55%) of the patients. The embolization materials used in all patients were a maximum of 15 ml lipiodol (Guerbet, Sulzbach, Germany), followed by the injection of 200–450 mg degradable starch microspheres (Embocept, Pharmacia & Upjohn, Erlangen, Germany). The embolization suspension was injected slowly under fluoroscopic control. After embolization, devascularization was confirmed by additional angiographic study of the hepatic artery. The study was designed to perform three courses of repetitive chemoembolization with treatment intervals of 4 weeks. With a satisfactory morphological response, the treatment was performed further for a longer extended course, sometimes up to 17 sessions.

Evaluation of morphological response

Control non-contrast and contrast-enhanced CT, and MRI for initial treatment planning were obtained for all patients. Twenty-four hours after embolization, retention of lipiodol in the tumor and the liver parenchyma was verified with noncontrast CT examination. CT was also important to detect non-target lipiodol emboli that might have refluxed during injection. All CT studies were performed using spiral technique on fourth-generation scanners (Somatom plus, Siemens, Erlangen, Germany). MRI using T1WI pre- and post-contrast and T2WI were performed in the pre-treatment phase using a 1.5-T MRI unit (Magnetom Symphony, Siemens, Erlangen, Germany). After every TACE cycle and after the end of the treatment course, non-contrast sagittal and axial T1W MRI studies were performed for evaluation of the size of the lesions. MRI offers, from our point of view, satisfactory contrast resolution without using contrast medium to judge the size of the lesions. Regarding the relatively large number of follow-up studies after each session, this was a practical choice reducing the radiation dose and the contrast medium load.

The change in size was calculated and the response judged according to RECIST criteria of tumor response to treatment. Tumor response is categorized by this method into complete response (CR), partial response (PR), stable disease (SD) and progressive disease (PD) based on measuring the sum of maximum diameters. The RECIST

CR is complete resolution of the lesions, while PR is defined as a 30% or more decrease in the sum of the diameters. The RECIST PD is defined as a 20% or more increase in the sum of the diameters of all lesions or the development of new lesions. Stable disease according to RECIST is defined by the range of changes falling between both PD and PR.

Statistical analysis

Statistical analysis was performed using BiAs 8.3.6 software. Survival times from the first diagnosis as well as from the start of treatment were both calculated to obtain the mean and median survival times and survival probability by using the Kaplan-Meier method. Survival probability was in terms of 5- and 10-year survival, dating from the first diagnosis, and 1- and 2-year survival probability dating from the start of TACE treatment. This difference between the two calculations is due to the fact that TACE was applied relatively late in the treatment course after other modalities were tried. Survival times were correlated to the number of sessions by dividing the patients into two groups: the first group received only three sessions, while the second received more than three sessions. Survival times dating from the first diagnosis and from the start of TACE were compared between the two groups using log-rank test. The same test was applied to the relation between survival times and tumor morphological response. We compared the survival times dating from the first diagnosis and from the start of TACE among patients showing SD and those showing PD.

Furthermore, we correlated the number of sessions to tumor response. Again, the patients were divided into two groups with those having only three sessions in the first and those with more than three sessions in the second. Tumor response outcomes were PR, SD and PD. The two variables were correlated using the Spearman rank correlation test and Kruskal-Wallis test. The patients treated by combined miotmycin and gemcitabine and those treated by miotmycin only were compared in terms of survival times using the log-rank test.

Results

Technical success was defined as successful selective catheterization of the feeding, segmental or lobar artery,

Table 1 Local tumor control outcome correlated to several influencing factors

Serial number	Gender	Age	Hepatic resection	Extrahepatic metastases	Number of sessions	Chemotherapeutic used	Local Response
1	Female	36	No	No	3	Only mitomycin	PD
2	Female	42	No	Thyroid	6	Only mitomycin	PD
3	Male	54	No	Lung	17	Only mitomycin	SD
4	Female	59	No	Lung	5	Gemcitabine and mitomycin	SD
5	Female	61	Yes	Lung	7	Gemcitabine and mitomycin	PD
6	Male	61	No	Lung	8	Only mitomycin	PR
7	Male	63	Yes	No	3	Gemcitabine and mitomycin	SD
8	Male	63	No	Lung	12	Only mitomycin	SD
9	Male	64	No	No	4	Gemcitabine and mitomycin	SD
10	Male	64	No	Lung, adrenal	6	Gemcitabine and mitomycin	PD
11	Male	65	No	Lung, pancreas, thyroid	3	Gemcitabine and mitomycin	SD
12	Female	65	No	Lung	4	Only mitomycin	SD
13	Female	65	Yes	Bone, spleen, IVC	4	Gemcitabine and mitomycin	SD
14	Male	66	Yes	Lung	3	Only mitomycin	PD
15	Male	67	No	Pancreas, spleen	11	Gemcitabine and mitomycin	SD
16	Female	67	No	Lung, skull	12	Gemcitabine and mitomycin	PR
17	Female	69	No	Lung	3	Only mitomycin	SD
18	Female	69	No	Bone	8	Gemcitabine and mitomycin	PD
19	Male	73	No	Lung	5	Gemcitabine and mitomycin	SD
20	Male	75	Yes	Lung	3	Only mitomycin	SD
21	Male	75	No	No	4	Gemcitabine and mitomycin	PR
22	Male	79	Yes	Lung	4	Only mitomycin	SD

PD = progressive disease, PR = partial response, SD = stable disease

according to tumor load and distribution, and subsequent complete injection of chemotherapeutic and embolizing agents. This was achieved in all patients.

Some of our patients suffered minor complications according to the criteria of the "Society of Vascular and Interventional Radiology." These were post-embolization syndrome in ten patients manifested by nausea, vomiting or right upper quadrant pain and a puncture site hematoma that resolved spontaneously in one patient. No major complications were encountered.

We followed up the effect of TACE as a symptomatic treatment measure in the eight symptomatic patients in our study. In three of the six patients having capsular pain, significant reduction of pain was observed after one session in one patient and after two sessions in the other two patients, leading to reduction of the required analgesic dose till the end of TACE sessions.

Only one of the three patients with biliary obstruction showed improved liver functions after four sessions of TACE, and the other two had to undergo endoscopic retrograde cholangio-pancreatography and stenting of the occluded central biliary ducts, which were complemented by further TACE sessions. The local control results in the four patients showing symptomatic improvement were partial response (PR) in one patient and stable disease (SD) in three patients.

Overall, partial response was achieved in 13.7%, stable disease in 59%, and progressive disease was encountered in 27.3% of the patients (Table 1; Figs. 1, 2 and 3). Of the 22 patients, 4 were still alive at the time of writing this work. Two of the 22 patients could not be located to confirm survival or date of death. These six patients were considered as censored during calculations of survival times and probabilities. Survival time dating from the diagnosis of metastases ranged from 18 and 307 months. Survival time dating from the start of TACE treatment ranged from 2.2 and 35 months. The median survival time estimated using the Kaplan-Meier method starting from the date of diagnosis of metastases was 67.6 months, while the mean survival time was 104.7 months. Using the same method, the median survival time from the start of the TACE course was 6.6 months, while the mean survival time was 10 months. Five- and 10-year survival probabilities starting from the date of diagnosis using the Kaplan-Meier method were 57 and 36%, respectively. Using the same method, survival probability from the start of treatment was 31% after 1 year and 6% after 2 years (Table 2).

The patients treated by combined miotmycin and gemcitabine and those treated by miotmycin were compared in terms of survival (Table 1). Survival times from the first diagnosis and from the start of TACE showed no statistical difference between the two groups using the log-rank test, having Cox-Mantel's chi values of 0.4236 (p=0.515149) and 0.6014 (p=0.438057), respectively (Fig. 4).

Another comparison of survival times was applied between patients undergoing only three sessions (the least applied in our institution) and those receiving more than three sessions. There was no statistical difference in

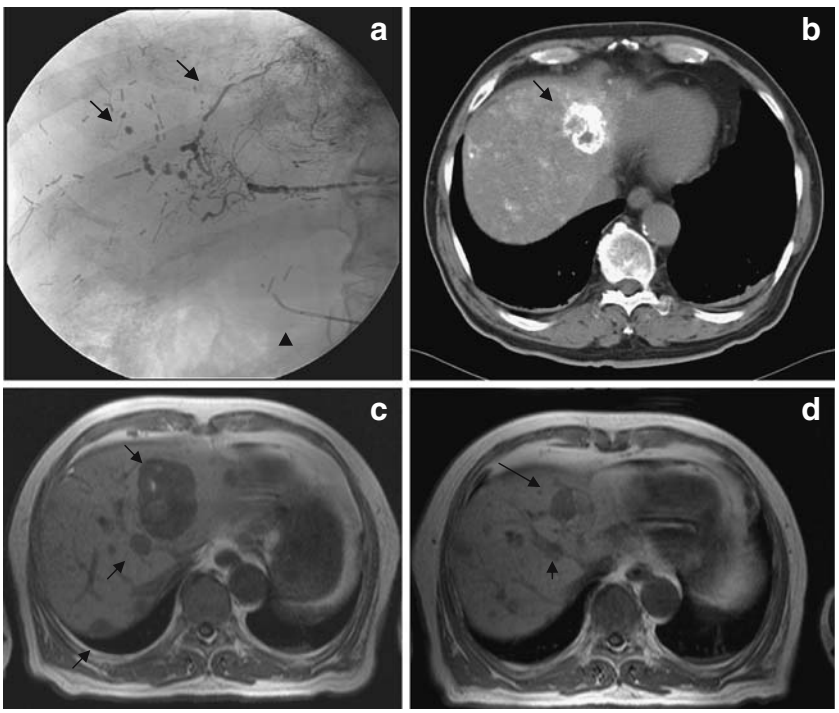

Fig. 1 A 46-year-old male patient showing partial response to TACE. **a** Hepatic artery lipiodol embolization using a Cobra catheter (arrowhead) in the hepatic artery proper after mitomycin intra-arterial perfusion. Lipiodol droplets are seen occluding the feeding arteries to the lesions in the left lobe (arrows). **b** Non-contrast CT abdomen showing lipiodol uptake by the largest lesion in the left lobe (arrow). **c** MRI of the liver before starting treatment. Pre-contrast axial T1WI showing multiple lesions in both hepatic lobes (arrows). **d** Partial response according to RECIST criteria after four TACE sessions. Control MRI axial T1WI showing more than 50% decrease in the sum of the lesions' largest diameters (arrows)

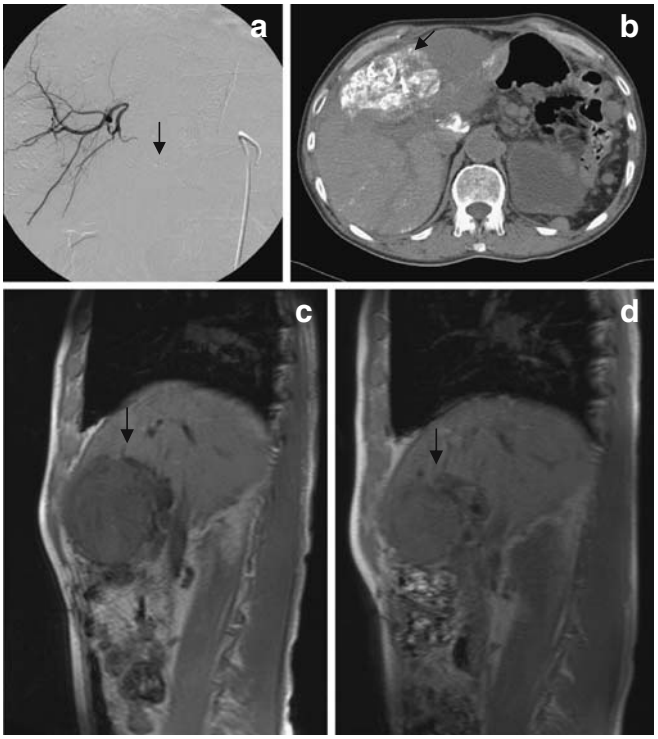

Fig. 2 A 51-year-old female patient showing stable disease after TACE. **a** Hepatic arteriogram using a Sos Omni catheter placed in the celiac trunk through which a 3F microcatheter (arrow) was introduced. **b** Non-contrast CT abdomen showing lipiodol uptake by the largest lesion lying in the left lobe (arrow). **c** MRI of the liver before starting treatment. Pre-contrast sagittal T1WI showing the same lesion (arrow). **d** Control MRI sagittal T1WI after four TACE sessions showing a decrease in the lesion size (arrow). However, this was a less than 50% decrease, hence making this a stable disease outcome by RECIST criteria

survival times dating from the first diagnosis and from the start of TACE. Cox-Mantel's chi values were 0.6015 (p=0.438003) and 0.2128 (p=0.644562), respectively.

The mean number of sessions was correlated with the local response (Table 3). This mean was 5.5 in PD, 6 in SD and 8 sessions in patients with PR. There was no statistically significant relation between the number of sessions and achieving partial morphological response using Spearman rank correlation test and Kruskal-Wallis test.

The mean survival time was correlated to tumor response. The mean survival time from the beginning of TACE in patients showing stable disease was 11.8 months, and in patients with progressive disease was 9.2 months. Using the log rank test, Cox-Mantel's chi was 0.1801 (p=0.671286). The mean survival time dating from the diagnosis of metastases in patients showing stable disease was 102.2 months and in patients with progressive disease was 83.3 months. Log rank test Cox-Mantel's chi was 0.8102 (p=0.368072). None of these calculated values is statistically significant.

Discussion

Renal cell carcinoma can metastasize to almost every organ of the body [16, 17]. Twenty-five to 30 percent of patients have overt metastases at initial presentation. Frequent sites include the lung parenchyma (50 to 60% of patients with metastases), bone (30 to 40%), liver (30 to 40%) and brain (5%). Unusual sites of metastases are characteristic of renal cancer, including the thyroid, pancreas, skeletal muscle, and skin or underlying soft tissue [17]. Absence of liver metastases was correlated with improved survival [18].

In a study of the behavior of renal cell carcinoma, the overall 5-year survival rates after simple and radical nephrectomy were 32% and 66.6%, respectively. It was found that radiation therapy cannot improve survival irrespective of stage. The 5-year survival rate with renal vein involvement was 32%. Nephrectomy in patients with distant metastasis did not alter survival. Among the patients with metastasis, 74% were dead before 1 year and 96% before 3 years [16].

Survival factors in another group of 86 patients with metastatic renal cell carcinoma were studied by computer analysis. Cumulative survival was 53% at 6 months, 43% at 1 year, 26% at 2 years and 13% at 5 years [19].

In another study, the 5-year survival rate was 31% in patients with metastatic renal cell carcinoma based on the interval from the time a metastasis was initially found to time of death. Eleven of the 16 patients (69%) with metastatic RCC had the primary tumor surgically removed at the time of diagnosis [20].

Liver metastases from renal cell carcinoma, like any other metastatic lesions, can be treated by surgery, systemic chemotherapy and radiotherapy, as well as image-guided interventional methods, which are broadly divided into percutaneous ablation and transarterial chemoperfusion, embolization and chemoembolization.

Surgical resection of liver metastases from renal cell carcinoma achieved survival rates for these patients that at 1 year ranged from 82.2% to 69% and at 3 years ranged from 26% to 54%, respectively. Median survival up to 48 months could be achieved [21–24]. The 3-year survival estimates for patients treated by chemotherapy and interferon were 15 and 48%, respectively [17].

The fact that our patients received systemic chemotherapy prior to TACE and that most, but not all had extrahepatic metastases makes the use of survival as an evaluation criterion for this treatment of less significance than local tumor control. We have achieved a favorable outcome in this regard in our study. We compared the size of lesions before starting TACE treatment, which was after ending systemic chemotherapy, to the size after treatment end. Thus, the effect of systemic chemotherapy on size was excluded. It can be assumed, at least theoretically, that reducing or stabilizing the bulk of the liver metastases

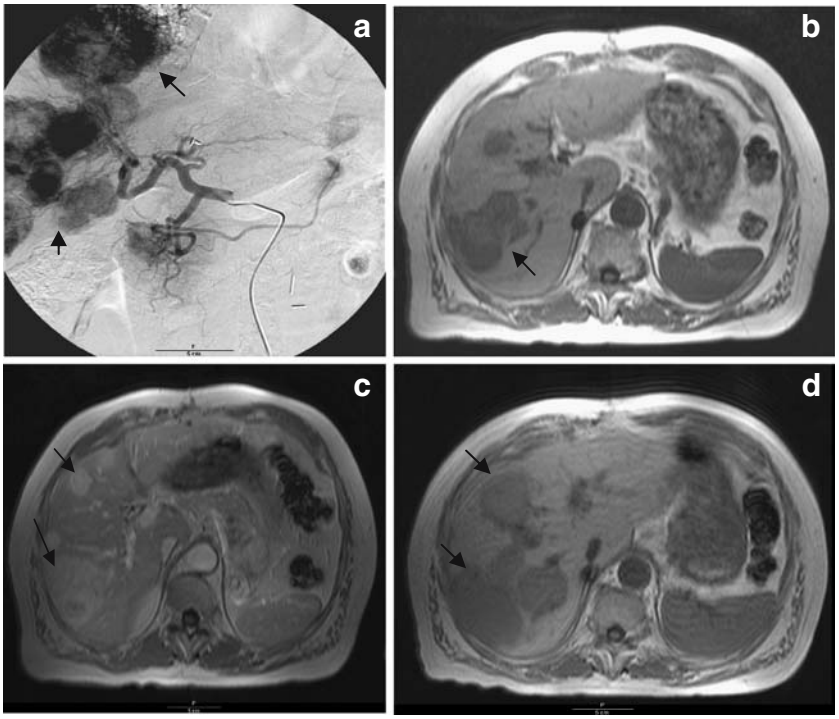

Fig. 3 A 62-year-old male patient showing progressive disease despite TACE. **a** Hepatic arteriogram using a Cobra catheter in the common hepatic artery demonstrating multiple variable-sized hypervascular liver metastases (arrows). **b, c** MRI of the liver before starting treatment. Post-contrast (B) and pre-contrast (C) axial T1WI showing multiple lesions in the right hepatic lobe with intense contrast enhancement (arrows). **d** In spite of initial response, control MRI axial T1WI after six TACE sessions showing increase in size and number of lesions after which TACE was stopped in favor of systemic chemotherapy (arrows)

Table 2 Survival times from diagnosis of liver metastases and from first diagnosis

Serial number	Date of birth	Date of 1st embolization	Date of 1st diagnosis of liver metastases	Date of death	Survival time from 1st TACE (days**)	Survival time from 1st diagnosis (months)
1	10.2.1965	29.5.2001	15*.3.2000	4.10.2001	125	18
2	16.2.1959	12.6.2001	15.1.1992	1.9.2002	438	120
3	16.6.1948	31.7.2002	15.2.1996	17.1.2003	167	67
4	2.9.1941	28.12.2000	15.1.1993	28.9.2001	280	105
5	26.12.1943	7.9.2004	15.11.2002	21.9.2005	374	35
6	14.5.1941	29.8.2001	15.7.1998	Lost to follow up		
7	7.8.1936	19.7.1999	15.11.1995	30.8.2001	761	70
8	10.12.1939	1.7.2002	15.10.1998	1.6.2003	330	128
9	16.9.1940	22.1.2004	15.3.1999	7.9.2004	225	65
10	22.11.1939	9.3.2005	15.1.1994	Lives		
11	4.4.1939	14.5.2004	15.1.1979	31.7.2004	77	307
12	14.3.1938	23.5.2003	15.12.1995	7.10.2003	134	69
13	21.9.1939	29.7.2004	15.7.2002	Lives		
14	13.2.1936	16.8.2002	15.2.1989	25.11.2002	96	154
15	4.6.1934	20.3.2001	15.8.1990	24.7.2002	484	157
16	7.3.1936	10.1.2003	15.1.1995	Lost to follow-up		
17	27.6.1932	16.8.2001	15.8.2000	2.12.2002	466	28
18	18.5.1934	19.12.2003	15.1.2001	1.7.2004	191	43
19	30.10.1932	9.3.2005	15.5.2002	1.7.2005	111	38
20	28.6.1927	1.11.2002	15.1.1996	Lives		
21	22.3.1930	22.7.2005	15.9.1995	Lives		
22	22.12.1923	11.3.2002	15.9.1999	1.10.2002	199	37

*Date of first diagnosis was known in terms of month and year without the exact day, and so the day was empirically assumed to be the 15th
**The survival time from the 1st diagnosis was calculated in days, then the mean and median were calculated

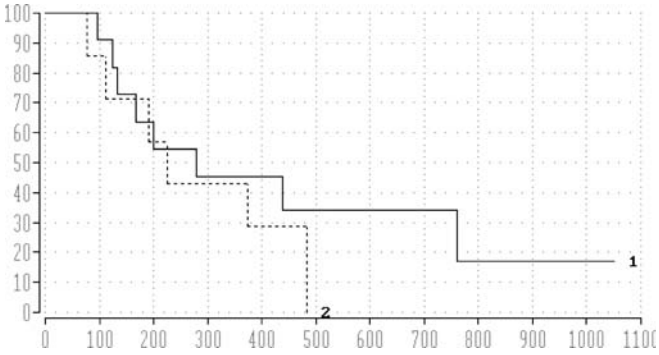

Fig. 4 Kaplan-Meier survival curves comparing the two chemotherapy regimens used in our study. Longitudenal axis represents the survival percentage correlated to survival time (in days) in the horizontal axis. Curve 1 represents the survival curve for patients treated by mitomycin only and curve 2 is for patients treated by mitomycin and gemcitabine. The two curves are overlapped together for comparison. Longer survival expectation could be achieved in mitomycin patients than those treated by combined protocol, yet this finding lacks statistical significance due to the small number of these patients

improves or maintains the liver function and hence the quality of life, regardless of its effect on survival.

The survival results achieved in our study were less favorable than those achieved by surgery; however, the patients selected for our study had more advanced liver involvement than those treated surgically. In our study we treated patients with up to 70% liver involvement, whereas in surgical resection the resectable lesions are usually less in number and more localized. The patients in our study started palliative TACE after exhausting other possibilities of treatment, including systemic chemotherapy, which makes the expectations not as high as in operable patients.

Moreover, the location of the lesions is of less importance in TACE; we can treat lesions in both lobes, however widespread they are, by selectively attacking the feeding arteries in the same or in separate sessions.

Survival benefit of TACE in liver metastases from RCC has to be better evaluated in a more specific group of patients. The problem in these patients is that the liver is usually not the sole site of metastases. Hence, a randomized controlled study comparing systemic chemotherapy to TACE is not feasible because lung metastases would not be tackled by TACE and will pose a likely cause of shorter survival in the TACE group.

There are several ways to overcome this problem that could be applied in future studies. First, a randomized controlled study comparing systemic chemotherapy to TACE in patients with hepatic metastases from renal cell carcinoma having no extrahepatic metastases can be attempted. Second, a randomized controlled study could compare systemic chemotherapy to combined TACE and systemic chemotherapy in patients with both hepatic and extra-hepatic metastases. A third method could be used in the subgroup of patients with metastases restricted to liver and lung only: after randomization, TACE of the liver and of the lung in one group could be performed, compared to systemic chemotherapy alone in a second group. TACE of lung metastases could be classically performed through the bronchial arteries and more recently through pulmonary arteries using a trans-femoral vein access [25].

This treatment protocol can also be modified into combined TACE of liver metastases and percutaneous radiofrequency or laser ablation of lung metastases if their size and number meet the criteria of this therapy.

Another point worth evaluation is the liver function and tumor markers, which can be evaluated simultaneously with survival and local tumor control in any of the above-mentioned proposed methods.

Conclusion

TACE can result in a favorable local tumor response in patients with hepatic metastases from RCC, but survival results are still limited.

Table 3 Number of sessions correlated to the response in individual patients

Number of sessions	Response
3	SD
3	SD
3	SD
3	SD
4	SD
4	SD
4	SD
4	SD
5	SD
5	SD
11	SD
12	SD
17	SD
4	PR
8	PR
12	PR
3	PD
3	PD
6	PD
6	PD
7	PD
8	PD

PD = progressive disease, PR = partial response, SD = stable disease

References

1. Voigt W, Behrmann C, Schlueter A, Kegel T, Grothey A, Schmoll HJ (2002) A new chemoembolization protocol in refractory liver metastasis of colorectal cancer: a feasibility study. Onkologie 25(2):158–164
2. Hunt TM, Flowerdew AD, Birch SJ, Williams JD, Mullee MA, Taylor I (1990) Prospective randomized controlled trial of hepatic arterial embolization or infusion chemotherapy with 5-fluorouracil and degradable starch microspheres for colorectal liver metastases. Br J Surg 77(7):779–782
3. Martinelli DJ, Wadler S, Bakal CW, Cynamon J, Rozenblit A, Haynes H, Kaleya R, Wiernik PH (1994) Utility of embolization or chemoembolization as second-line treatment in patients with advances or recurrent colorectal carcinoma. Cancer 74(6):1706–1712
4. Muller H, Nakchbandi V, Chatzisavvidis I, von Voigt C (2003) Repetitive chemoembolization with melphalan plus intraarterial immunochemotherapy within 5-fluorouracil and granulocyte-macrophage colony-stimulating factor (GM-CSF) as effective first- and second-line treatment of disseminated colorectal liver metastases. Hepatogastroenterology 50 (54):1919–1926
5. Wasser K, Giebel F, Fischbach R, Tesch H, Landwehr P (2005) Transcatheter arterial chemoembolization of colorectal liver metastases using degradable starch microspheres (Spherex (R)). Own investigations and review to the literature. [German] Radiologe 45 (7):633–643
6. Tarazov PG (2000) Transcatheter therapy of gastric cancer metastatic to the liver: preliminary results. J Gastroenterol 35(12):949–950
7. Taniguchi H, Takahashi T, Sawai K, Yamaguchi T, Hagiwara A, Kitamura K et al (1997) Comparison in survival between hepatic metastases of gastric and colorectal cancers. Hepatogastroenterology 44(15):897–900
8. Fromigue J, De Baere T, Baudin E, Dromain C, Leboulleux S, Schlumberger M (2006) Chemoembolization for liver metastases from medullary thyroid carcinoma. J Clin Endocrinol Metab 91(7):2496–2499 Jul
9. Lorenz K, Brauckhoff M, Behrmann C, Sekulla C, Ukkat J, Brauckhoff K, Gimm O, Dralle H (2005) Selective arterial chemoembolization for hepatic metastases from medullary thyroid carcinoma. Surgery 138(6):986–993 Dec
10. Roche A, Girish BV, de Baere T, Baudin E, Boige V, Elias D, Lasser P, Schlumberger M, Ducreux M (2003) Transcatheter arterial chemoembolization as first-line treatment for hepatic metastases from endocrine tumors. Eur Radiol 13(1):136–140
11. Fiorentini G, Rossi S, Bonechi F, Vaira M, De Simone M, Dentico P, Bernardeschi P, Cantore M, Guadagni S (2004) Intraarterial hepatic chemoembolization in liver metastases from neuroendocrine tumors: a phase II study. J Chemother 16 (3):293–297
12. Kress O, Wagner HJ, Wied M, Klose KJ, Arnold R, Alfke H (2003) Transarterial hemoembolization of advanced liver metastases of neuroendocrine tumors-a retrospective single-center analysis. Digestion 68(2–3):94–101
13. Agarwala SS, Panikkar R, Kirkwood JM (2004) Phase I/II randomized trial of intrahepatic arterial infusion chemotherapy with cisplatin and chemoembolization with cisplatin and polyvinyl sponge in patients with ocular melanoma metastatic to the liver. Melanoma Res 14(3):217–222
14. Bedikian AY, Legha SS, Mavligit G, Carrasco CH, Khorana S, Plager C, Papadopoulos N, Benjamin RS (1995) Treatment of uveal melanoma metastatic to the liver: a review of the MD Anderson Cancer Center experience and prognostic factors. Cancer 76 (9):1665–1670
15. Yayoi E, Furukawa J, Sekimoto M, Kinuta M, Tateishi H, Maruyama H, Okamura J, Ooi H (1995) A comparison of intra-arterial chemoembolization and infusion chemotherapy for liver metastases of breast cancer. Gan To Kagaku Ryoho 22(11):1519–1522 Sep
16. Patel NP, Lavengood RW (1978) Renal cell carcinoma: natural history and results of treatment. J Urol 119(6):722–726 Jun
17. Motzer RJ, Bander NH, Nanus DM (1996) Renal-cell carcinoma. N Engl J Med 335(12):865–875
18. Fossa SD, Kramar A, Droz JP (1994) Prognostic factors and survival in patients with metastatic renal cell carcinoma treated with chemotherapy or interferon-alpha. Eur J Cancer 30A (9):1310–1314
19. Dekernion JB, Ramming KP, Smith RB (1978) The natural history of metastatic renal cell carcinoma: a computer analysis. J Urol 120(2):148–152 Aug
20. Toshiro O, Noriomi M, Atsushi T et al (2001) Growth rates of primary and metastatic lesions of renal cell carcinoma. Int J Urol 8:473–477
21. Kawata N, Hirakata H, Yuge H et al (2000) Cytoreductive surgery with liver-involved renal cell carcinoma. Int J Urol 7(10):382–385 Oct
22. Fujisaki S, Takayama T, Shimada K et al (1997) Hepatectomy for metastatic renal cell carcinoma. Hepatogastroenterology 44(15):817–819 May-Jun
23. Alves A, Adam R, Majno P et al (2003) Hepatic resection for metastatic renal tumors: is it worthwhile? Ann Surg Oncol 10(6):705–710 Jul
24. Thelen A, Jonas S, Benckert C, Lopez-Hänninen E, Rudolph B, Neumann U, Neuhaus P (2007) Liver resection for metastases from renal cell carcinoma. World J Surg 31(4):802–807 Apr
25. Vogl TJ, Wetter A, Lindemayr S, Zangos S (2005) Treatment of unresectable lung metastases with transpulmonary chemoembolization: preliminary experience. Radiology 234(3):917–922 Mar