平成１９年度～２１年度

厚生労働科学研究費補助金
医療技術実用化総合研究事業
転移性骨腫瘍に対する経皮的ラジオ波凝固療法に関する研究

総合研究報告書

研究代表者　荒井　保明

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別紙２

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Ⅰ.総合研究報告

別紙３

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転移性骨腫瘍に対する経皮的ラジオ波凝固療法に関する研究

研究代表者　荒井保明　国立がんセンター中央病院　放射線診断部部長

研究要旨
がん患者の QOL 向上をめざした IVR 技術を開発・評価するために、多施設共同臨床試験組織 JIVROSG（日本腫瘍 IVR 研究グループ）により行われていた臨床試験「転移性骨腫瘍に対する経皮的ラジオ波凝固療法に関する第Ⅰ/Ⅱ相試験（JIVROSG-0208）」を高度医療評価制度（当初「臨床的な使用確認試験として開始）」として継続して行った。目標症例数 33 例のうち 30 例の登録を完了し、平成 22 年中に試験の完遂が見込まれ、有痛性骨腫瘍に対する経皮的ラジオ波凝固療法の安全性、有効性について信頼性の高いデータが提示できるものと予測される。

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A. 研究目的

本研究は、骨腫瘍に対する経皮的ラジオ波凝固療法(radiofrequency ablation: RFA)が平成 19 年度末にて先進医療から除外されたことを受け、厚生労働省が提唱した「臨床的な使用確認試験（平成 20 年度より高度医療評価制度に移行）」として、日本腫瘍 IVR グループ(JIVROSG)が開始していた「転移性骨腫瘍に対する経皮的 RFA についての第Ⅰ/Ⅱ相臨床試験(JIVROSG-0208)」を継承する形で行ったものである。Interventional radiology(以下 IVR)は画像誘導下に経皮的手技により治療を行うものであり、その迅速性、低侵襲性から、がん治療、特に QOL を考慮したがん治療における高い有効性が期待されているが、標準的治療として実臨床に導入されるためには科学的な評価が乏しい。かくて、本研究の目的は、有痛性転移性骨腫瘍に対する経皮的 RFA の安全性ならびに臨床的有効性を主評価項目を、安全性の評価、副次的評価項目を臨床的有効性と有害事象の発現頻度と程度の評価とし、これを多施設共同研究により評価することにある。

B. 研究方法

JIVROSG に参加する 24 施設が参加して行った。症例登録は大学病院医療情報ネットワーク（UMIN）内のホームページの研究者限定サイトからのオンライン登録とし、データマネージメントは臨床試験のデータマネージメントを専門とする企業に外部委託した。第Ⅰ相試験部分については、技術である IVR の安全性について初期段階で評価する既存の方法がないため、薬物療法における第Ⅰ相試験の概念を模し、3 例を一段階として 4 週の観察期間をおき、重篤な有害事象頻度 1/3 以下を確認後次段階に進み、3 段階 9 例の終了時点で第Ⅱ相試験に進むための安全性を最終評価する方法（JIVROSG 3×3 法）を採用した。本研究の試験の概要は以下の如くである。

１）評価項目
主要評価項目：安全性の評価。
副次的評価項目：臨床的有効性の評価。有害事象の発現頻度と程度。

２）症例選択規準
①疼痛を主訴とする臨床症状を有する転移性骨腫瘍症例であり、かつ従来の局所治療法が適応とならないか奏効しなかった症例、あるいは鎮痛剤の増量でしか疼痛のコントロールができない症例。②対象病変が組織学的あるいは画像診断上、悪性であることが確認されている。③対象病変がＣＴあるいは MRI により評価可能である。④主要臓器（骨髄、心、肝、肺、腎など）機能が保持されている症例。⑤P.S.　(ECOG)：０，１，２，３。⑥４週間以上の生存が見込める。⑦患者本人から文書による同意が得られている、の条件をすべて満たす症例。

３）治療
画像ガイド下に経皮的にラジオ波電極針を腫瘍に穿刺し、腫瘍に対してラジオ波による凝固療法を施行する。

４）評価方法
有害事象については NCI-CTC Ver.2 を用い、有効性は、薬物療法の影響を排除した VAS 値の変化により評価する。

４）予定登録数と研究期間、予定登録数：３３例。登録期間：４８ヶ月。追跡期間：登録終了後３ヶ月。総研究期間：５１ヶ月。

(倫理面への配慮)
ヘルシンキ宣言を遵守し、これをプロトコールに

明記し、文書を用いた説明と患者本人からの文書による同意取得を必須とした。また、プロトコールは、日本ＩＶＲ学会倫理委員会による承認と、さらにその後に参加施設の施設倫理審査委員会あるいは IRB にて承認を得ることを必須とした。個人情報の保護については、試験の信頼性を確保するためオンライン登録時にのみ個人情報を使用し、以後はすべて試験番号－症例登録番号のみで運営することとした。なお、オンライン登録時に使用された患者個人情報は不正なアクセスへの対策が講じられた UMIN インターネット医学研究データセンターのコンピュータ内に保存され、このデータへのアクセス権限は、グループ代表者、研究代表者、データセンター代表者、グループ内 UMIN 担当者、UMIN 内 JIVROSG 担当者の 5 名のみが有し、試験遂行に必要な場合にのみアクセスすることとし、かつそのアクセスもすべて記録保存されるシステムとした。

C. 研究結果

9 例にて第 I 相試験部分を終了した。重篤な有害事象の発現はなく、プロトコールに定めた規定に従って第 II 相試験部分に移行して試験が継続された。この結果、平成 22 年度末までに予定症例数 33 例中 30 例が登録された。ちなみに、症例登録速度は高度医療評価制度に移行する前の 3 年 1 カ月に 9 例であったのに対し、移行後の 2 年 6 カ月で 21 例と増加した。これまで重篤な有害事象の発生は認めれ宛ていない。臨床試験としての性格上、予定症例数登録完了以前の段階での有害事象以外についての集計・公表は好ましくないため、有効性については明らかにできないが、有効例が多数存在する点は定期モニタリングで確認されている。目標症例数 33 例が平成 22 年中に完遂されることが確実視される状況であり、症例登録が完了され次第、データ固定、解析完了が見込まれる。

D. 考察

低侵襲治療とされる IVR については、特に QOL を考慮したがん治療を行う上で、その有用性に大きな期待が持たれているが、海外も含めこれまで臨床試験による評価は行われていない。このため、転移性骨腫瘍に対する経皮的ラジオ波凝固療法についての評価を多施設共同臨床試験で行う本研究は、先進的であり、かつ意義の大きなものであったと考えられる。本年度の研究により、本研究の完遂が確実に見込める状況となり、有痛性骨腫瘍に対する経皮的ラジオ波凝固療法についての信頼性の高い安全性、有効性のデータが提示されることが期待される。一方、有効な IVR を臨床現場に効率的に導入するためには、機器ならびに手技について、行政による承認と診療報酬上の適正な処理が必須であり、この点では、本臨床試験が高度医療評価制度に組み込まれて行われたことは、大きな意義をもつと考えられる。実際、症例集積速度は高度医療評価制度に組み込まれた時期を境に、明らかに増加し、また、本研究費によりデータマネージメントのアウトソーシングが可能となったことによりデータの信頼性が著しく向上した。この事実は、新規治療技術や新規治療機器の導入過程における競争的公的研究費の有効利用や IVR 関係の臨床試験と行政との関わりについても重大な示唆を示したものと考えられる。

E. 結論

有痛性転移性骨腫瘍に対する経皮的 RFA についての第 I /II 相臨床試験(JIVROSG-0208)を継続して行い、研究期間中に予定症例数 33 例中 30 症例までが登録され、試験の平成 22 年内の完了が確実となった。重篤な有害事象の発現はなく、多数の有効例の存在が確認されており、有痛性骨腫瘍に対する経皮的ラジオ波凝固療法の安全性、有効性について信頼性の高いデータが確実に提示できるものと予測される。

F. 健康危険情報

なし。

G. 研究発表

1.論文発表

1) Inaba Y, Arai Y, Aramaki T, et al. Phase I/II Study of Hepatic Arterial Infusion Chemotherapy With Gemcitabine in Patients With Unresectable Intrahepatic Cholangiocarcinoma (JIVROSG-0301). Am J Clin Oncol. 2010 Feb 19. [Epub ahead of print]

2) Tokue H, Tsushima Y, Arai Y, et al. Jejunogastric intussusception: life-threatening complication occuring 55 years after gastrojejunostomy. Intern Med. 48:1657-60, 2009

3) Sofue K, Tateishi U, Arai Y, et al. Role of carbon-11 choline PET/CT in the management of uterine carcinoma: initial experience. Ann Nucl Med. 23:235-43, 2009

4) Hirokawa T, Sawai H, Arai Y, et al. Middle-colic artery aneurysm associated with segmental arterial mediolysis, successfully managed by transcatheter arterial embolization: report of a case. Surg Today. 39:144-7, 2009

5) Kobayashi T, Arai Y, Takeuchi Y, et al: Phase I/II clinical study of percutaneous vertebroplasty (PVP) as palliation for painful malignant vertebral compression fractures (PMVCF): JIVROSG-0202. Ann Oncol. 20:1943-7, 2009

6) Tokuda T, Tanigawa N, Kariya S, et al. Pancreatitis after transcatheter embolization of a splenic aneurysm. Jpn J Radiol 28:239-42, 2010

7) Suzuki S, Tanigawa N, Kariya S, et al. Posterior

Reversible Encephalopathy Syndrome Occurring After Cardiovasc Intervent Radiol 2010 Feb 12. [Epub ahead of print]
8) Kashima M, Yamakado K, Tanigawa N, et al. Radiofrequency ablation for the treatment of bone metastases from hepatocellular carcinoma. AJR Am J Roentgenol 194:536-41, 2010
9) Tokuda T, Tanigawa N, Shomura Y, et al. Transcatheter embolization for peripheral pseudoaneurysms with n-butyl cyanoacrylate. Minim Invasive Ther Allied Technol 18:361-5, 2009
10) Tanigawa N, Kariya S, Komemushi A, et al. Cement leakage in percutaneous vertebroplasty for osteoporotic compression fractures with or without intravertebral clefts. AJR Am J Roentgenol 193:W442-5, 2009
11) Tokuda T, Tanigawa N, Shomura Y,et al. Transcatheter embolization for peripheral pseudoaneurysms with n-butyl cyanoacrylate. Minim Invasive Ther Allied Technol 1:1-5, 2009
12) Satoi S, Yanagimoto H, Tanigawa N, et al. Pre-operative patient selection of pancreatic cancer patients by multi-detector row CT. Hepatogastroenterology 56:529-34, 2009
13) Tokuda T, Shomura Y, Tanigawa N, et al. Mechanical characteristics of composite knitted stents. Cardiovasc Intervent Radiol 32:1028-32, 2009
14) Kariya S, Tanigawa N, Kojima H, et al. Percutaneous translumbar inferior vena cava cannulation under computed tomography guidance. Jpn J Radiol 27:176-9, 2009
15) Kariya S, Tanigawa N, Kojima H, et al. Peripheral stent placement in hemodialysis grafts. Cardiovasc Intervent Radiol 32:960-6, 2009
16) Satoi S, Yanagimoto H, Tanigawa N, et al. Surgical results after preoperative chemoradiation therapy for patients with pancreatic cancer. Pancreas 38:282-8, 2009
17) Tanigawa N, Kariya S, Kojima H, et al. Transcatheter coil embolization of an aneurysm of an anomalous splenic artery: usefulness of double microcatheter method. Minim Invasive Ther Allied Technol 18:311-4, 2009
18) Kojima H, Tanigawa N, Kariya S, et al. High-flow priapism undergoing arterial embolization: review of literature following American Urological Association guideline on the management of priapism. Minim Invasive Ther Allied Technol 18:1-5, 2009
19) Takizawa K, Shimamoto H, Nakajima Y, et al. Development of a new subclavian arterial infusion chemotherapy method for locally or recurrent advanced breast cancer using an implanted catheter-port system after redistribution of arterial tumor supply. Cardiovasc Intervent Radiol. 32:1059-66, 2009
20) Suenaga M, Mizunuma N, Matsueda K, et al. Management of venous thromboembolism in colorectal cancer patients treated with bevacizumab. Med Oncol 2009 [Epub ahead of print]
Uterine Artery Embolization for Uterine Myoma. print]
21) Shitara K, Matsuo K, Inaba Y, et al. Neutropaenia as a prognostic factor in metastatic colorectal cancer patients undergoing chemotherapy with first-line FOLFOX. Eur J Cancer. 45:1757-63, 2009
22) Iguchi T, Arai Y, Inaba Y, et al. Hepatic arterial infusion chemotherapy through a port-catheter system as preoperative initial therapy in patients with advanced liver dysfunction due to synchronous and unresectable liver metastases from colorectal cancer. Cardiovasc Intervent Radiol 31:86-90, 2008
23) Miyake M, Tateishi U, Arai Y, et al. Computed tomography and magnetic resonance imaging findings of soft tissue perineurioma. Radiat Med 26:368-71, 2008
24) Morimoto T, Iinuma G, Arai Y, et al. Computer-aided detection in computed tomographycolonography: current status and problems with detection of early colorectal cancer. Radiat Med 26:261-9, 2008
25) Satake M, Uchida H, Arai Y, et al. Transcatheter arterial chemoembolization (TACE) with lipiodol to treat hepatocellular carcinoma: survey results from the TACE study group of Japan. Cardiovasc Intervent Radiol 31:756-61, 2008
26) Sakaino S, Takizawa K, Nakajima Y et al. Percutaneous vertebroplasty performed by the isocenter puncture method. Radiat Med 26:70-5, 2008
27) Komemushi A, Tanigawa N, Kariya S, et al. Biochemical markers of boneturnover in percutaneous vertebroplasty for osteoporotic compressionfracture. Cardiovasc Intervent Radiol 31:332-5, 2008
28) Saito Y, Nobuhara K, Tanigawa N, et al. The corpus callosum in obsessive-compulsive disorder: a diffusion tensor imaging study. Radiology 246:536-42, 2008
29) Sugimoto T, Tanigawa N, Ikeda K, et al. Diffusion-weighted imaging for predicting new compression fractures following percutaneous vertebroplasty. Acta Radiologica 49:419-26, 2008
30) Tanigawa N, Kariya S, Kojima H, et al. Improvement in respiratory function by percutaneous vertebroplasty. Acta Radiologica 49:638-43, 2008
31) Komemushi A, Tanigawa N, Kariya S, et al. Intraosseous Venography with Carbon Dioxide in Percutaneous Vertebroplasty: Carbon Dioxide Retention in Renal Veins. Cardiovasc Intervent Radiol.31:1174-7, 2008
32) Takaoka E,Sekido N, Matsueda K, et al. Cavernous hemangioma mimicking a cystic renal cell carcinoma. Int J Clin Oncol 13:166-8, 2008.
33) Seki M, Ninomiya E, Matsueda K, et al. Pancreatogram findings for carcinoma in situ (CIS) of the pancreas seen on endoscopic retrograde cholangiopancreatography and postoperative pancreatography of resected specimens: can CIS be diagnosed preoperatively? Pancreatology 8:142-52, 2008
34) Akiyoshi T, Oya M, Matsueda K, et al. Comparison

of preoperative whole-body positron emission tomography with MDCT in patients with primary colorectal cancer. Colorectal Dis. 11:464-9, 2009
35) Matsushima S, Nishiofuku H, Inaba Y, et al. Equivalent Cross-Relaxation Rate Imaging of Axillary Lymph Nodes in Breast Cancer. J Magn Reson Imaging 27:1278-83, 2008
36) Yamaura H, Inaba Y, Sato Y, et al. Bilateral pneumothorax after unilateral transthoracic puncture. J Vasc Interv Radiol 18:793-5, 2008
37) Tahara M, Shirao K, Inaba Y, et al. Multicenter Phase II study of cetuximab plus irinotecan in metastatic colorectal carcinoma refractory to irinotecan, oxaliplatin and fluoropyrimidines. Jpn J Clin Oncol 38:762-9, 2008
38) Arai Y, Takeuchi Y, Inaba Y, et al. Percutaneous catheter placement for hepatic arterial infusion chemotherapy. Tech Vasc Interv Radiol.10:30-7, 2007
39) Tateishi U, Hosono A, Arai Y, et al. Accuracy of 18F fluorodeoxyglucose positron emission tomography/computed tomography in staging of pediatric sarcomas. Pediatr Hematol Oncol. 29:608-12, 2007
40) Shimamoto H, Inaba Y, Arai Y, et al. Chest wall dissemination of nocardiosis after percutaneous transthoracic needle biopsy. Cardiovasc Intervent Radiol. 30:797-9, 2007
41) Ishizumi T, Tateishi U, Arai Y, et al. F-18 FDG PET/CT imaging of low-grade mucoepidermoid carcinoma of the bronchus. Ann Nucl Med.21:299-302, 2007
42) Maeda T, Tateishi U, Arai Y, et al. Primary hepatic angiosarcoma on coregistered FDG PET and CT images. AJR Am J Roentgenol. 188:1615-7, 2007
43) Maeda T, Tateishi U, Arai Y, et al. Unsuspected bone and soft tissue lesions identified at cancer screening using positron emission tomography. Jpn J Clin Oncol. 37:207-15, 2007
44) Sakamoto N, Monzawa S, Arai Y, et al. Acute tumor lysis syndrome caused by transcatheter oily chemoembolization in a patient with a large hepatocellular carcinoma. Cardiovasc Intervent Radiol. 30:508-11, 2007
45) Tanigawa N, Komemushi A, Kariya S, et al. Relationship between cement distribution pattern and new compression fracture after percutaneous vertebroplasty. Am J Roentgenol 189:W348-352, 2007
46) Tanigawa N, Kariya S, Kojima H, et al. Lower limb ischemia caused by fractured osteochondroma of the femur. Br J Radiol 80:e78-e80, 2007
47) Kariya S, Tanigawa N, Kojima H, et al. Primary patency with cutting and conventional balloon angioplasty for different types of hemodialysis access stenosis. Radiology 243:578-87, 2007
48) Satoi S, Yamamoto H, Tanigawa N, et al. Clinical impact of multidetector row computed tomography on patients with pancreatic cancer. Pancreas 34:175-179, 2007
49) Yamakado K, Hase S, Tanigawa N, et al. Radiofrequency ablation for the treatment of unresectable lung metastases in patients with colorectal cancer: a multicenter study in Japan. J Vasc Interv Radiol 18:393-398, 2007
50) Kanemaki Y, Kurihara Y, Nakajima Y, et al. Ductal Carcinoma in Situ :Correlations between High-resolutin Magnetic Resonance Imaging and Histopathology. Radiat Med 25:1-7, 2007
51) Zhu Z, Kurihara Y, Nakajima Y, et al. Diagnostic Accuracy of High-Resolution MRI Using a Microscopy Coil for Patients with Presumed DCIS Following Mammography Screening. J Magn Reson Imaging 25:96-103, 2007
52) Matsuoka S, Kurihara Y, Nakajima Y, et al. Quantitative Thin-Section CT Analysis of the Enlargement and Coalescence of Low-Attenuation Clusters in Patients with Emphysema. Respiration. 136-141, 2007
53) Yamaura H, Inaba Y, Sato Y, et al. Bilateral pneumothorax after unilateral transthoracic puncture. J Vasc Interv Radiol.18:793-795,2007.
54) Inaba Y, Yamaura H, Sato Y, et al. Central Venous Access Port-related Complications in Outpatient Chemotherapy for Colorectal Cancer. Jpn J Clin Oncol.37:951-954,2007.
55) Shimamoto H, Inaba Y, Arai Y, et al. Chest wall dissemination of nocardiosis after percutaneous transthoracic needle biopsy. Cardiovasc Intervent Radiol.30:797-899, 2007.

H. 知的財産権の出願・登録状況
1.特許取得
なし
2.実用新案登録
なし
3.その他
なし

II. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書　籍　名	出版社名	出版地	出版年	ページ
稲葉吉隆, 森田荘二郎, 新槇　剛	ポートの管理法	荒井保明, 森田荘二郎, 竹内義人, 稲葉吉隆, 新槇　剛	中心静脈ポートの使い方	南江堂	東京	2008	55-70
佐藤洋造, 稲葉吉隆, 山浦秀和, 名嶋弥菜	血管造影の役割	中川和彦	Cancer Treatment Navigator	メディカルレビュー社	東京	2008	64-65
稲葉吉隆	IVRにおける合併症とその対策	武藤徹一郎	ガイドラインサポートブック大	医薬ジャーナル社	東京	2008	88-90
新槇 剛	中心静脈ポートの使い方	荒井保明, 竹内義人, 稲葉吉隆, 新槇 剛, 森田荘二郎	中心静脈ポートの使い方	南江堂	東京	2008	
稲葉吉隆	大腸癌治療のためのQ&A:肝動注療法の有用性、その適応は？	杉村健一	ガイドラインサポートハンドブック大腸癌：大腸癌治療ガイドライン2009年版	医薬ジャーナル社	大阪	2010	238
稲葉吉隆	抗がん薬の投与方法：ポートの留置・管理	日本臨床腫瘍学会	新臨床腫瘍学改訂第2版	南江堂	東京	2009	404-407

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Iguchi T, Arai Y, Inaba Y, et al.	Hepatic arterial infusion chemotherapy through a port-catheter system as preoperative initial therapy in patients with advanced liver dysfunction due to synchronous and unresectable liver metastases from colorectal cancer.	Cardiovasc Intervent Radiol	31	86-90	2008

Miyake M, Tateishi U, Arai Y, et al.	Computed tomography and magnetic resonance imaging findings of soft tissue perineurioma.	Radiat Med	26	368-71	2008
Morimoto T, Iinuma G, Arai Y, et al.	Computer-aided detection in computed tomographycolonography: current status and problems with detection of early colorectal cancer.	Radiat Med	26	261-9	2008
Satake M, Uchida H, Arai Y, et al.	Transcatheter arterial chemoembolization (TACE) with lipiodol to treat hepatocellular carcinoma: survey results from the TACE study group of Japan.	Cardiovasc Intervent Radiol	31	756-61	2008
Sakaino S, Takizawa K, Nakajima Y, et al.	Percutaneous vertebroplasty performed by the isocenter puncture method.	Radiat Med	26	70-5	2008
Komemushi A, Tanigawa N, Kariya S, et al.	Biochemical markers of boneturnover in percutaneous vertebroplasty for osteoporotic compressionfracture.	Cardiovasc Intervent Radiol	31	332-5	2008
Saito Y, Nobuhara K, Tanigawa N, et al.	The corpus callosum in obsessive-compulsive disorder: a diffusion tensor imaging study.	Radiology	246	536-42	2008
Sugimoto T, Tanigawa N, Ikeda K, et al.	Diffusion-weighted imaging for predicting new compression fractures following percutaneous vertebroplasty.	Acta Radiologica	49	419-26	2008
Tanigawa N, Kariya S, Kojima H, et al.	Improvement in respiratory function by percutaneous vertebroplasty.	Acta Radiologica	31	638-43,	2008
Komemushi A, Tanigawa N, Kariya S, et al.	Intraosseous Venography with Carbon Dioxide in Percutaneous Vertebroplasty: Carbon Dioxide Retention in Renal Veins.	Cardiovasc Intervent Radiol	31	1174-7	2008
Takaoka E, Sekido N, Matsueda K, et al.	Cavernous hemangioma mimicking a cystic renal cell carcinoma.	Int J Clin Oncol	13	166-8	2008

Seki M, Ninomiya E, Matsueda K, et al.	Pancreatogram findings for carcinoma in situ (CIS) of the pancreas seen on endoscopic retrograde cholangio-pancreatography and postoperative pancreatography of resected specimens: can CIS be diagnosed preoperatively?	Pancreatology	8	142-52	2008
Matsushima S, Nishiofuku H, Inaba Y, et al.	Equivalent Cross-Relaxation Rate Imaging of Axillary Lymph Nodes in Breast Cancer.	J Magn Reson Imaging	27	1278-83	2008
Yamaura H, Inaba Y, Sato Y, et al.	Bilateral pneumothorax after unilateral transthoracic puncture.	J Vasc Interv Radiol	18	793-5	2008
Tahara M, Shirao K, Inaba Y, et al.	Multicenter Phase II study of cetuximab plus irinotecan in metastatic colorectal carcinoma refractory to irinotecan, oxaliplatin and fluoropyrimidines.	Jpn J Clin Oncol 38:762-9, 2008	38	762-9	2008
中島康雄　他	Percutaneous vertebroplasty performed by the isocenter puncture method.	Radiat Med.	26(2)	70-5	2008
Tanigawa N, Kariya S, Kojima H, et al.	Improvement in respiratory function by percutaneous vertebroplasty	Acta Radiologica	49(6)	638-643	2008
Komemushi A, Tanigawa N, Kariya S, et al.	Intraosseous Venography with Carbon Dioxide in Percutaneous Vertebroplasty: Carbon Dioxide Retention in Renal Veins	Cardiovasc Intervent Radiol	31(6)	1174-1177	2008
Saito Y, Nobuhara K, Okugawa G, Takase K, Sugimoto T, Horiuchi M, Ueno C, Maehara M, Omura N, Kurokawa H, Ikeda K, Tanigawa N, Sawada S.	Corpus callosum in patients with obsessive-compulsive disorder: a diffusion-tensor imaging study	Radiology	246(2)	536-542,	2008
Komemushi A, Tanigawa N, Kariya S, et al.	Biochemical markers of boneturnover in percutaneous vertebroplasty for osteoporotic compressionfracture.	Cardiovasc Intervent Radiol	31(2)	332-335	2008
Sugimoto T, Tanigawa N, Ikeda K, et al.	Diffusion-weighted imaging for predicting new compression fractures following percutaneous vertebroplasty.	Acta Radiologica	49(4)	419-426	2008

Tanigawa N, Kariya S, Kojima H, et al.	Cerebral microembolization during radiofrequency ablation of lung tumors: Detection by carotid duplex ultrasound	Br J Radiol.	82(975)	249-253	2009
Kariya S, Tanigawa N, Kojima H, et al.	Transcatheter Coil Embolization of Collateral Veins for Steal Syndrome Associated with Hemodialysis Access Originating in Brachial Artery	Acta Radiologica	50(1)	28-33	2009
Iguchi T, Arai Y, Inaba Y, et al	Hepatic arterial infusion chemotherapy through a port-catheter system as preoperative initial therapy in patients with advanced liver dysfunction due to synchronous and unresectable liver metastases from colorectal cancer.	Cardiovasc Intervent Radiol.	31	86-90	2008
Matsushima S, Inaba Y, et al	Equivalent cross-relaxation rate imaging of axillary lymph nodes in breast cancer.	J Magn Reson Imaging	27	1278-1283	2008
稲葉吉隆，山浦秀和，佐藤洋造，名嶋弥菜	皮下埋め込み型中心静脈リザーバー（CV ポート）の造設方法と合併症対策	看護技術	54	348-351	2008
佐藤洋造，稲葉吉隆，山浦秀和，他	肝術後難治性腹水に対し TIPS を施行した 1 例	IVR	24Suppl e	6-7	2009
稲葉吉隆，山浦秀和，佐藤洋造，他	体腔内液体貯留に対する経皮的ドレナージ	IVR	24	61-65	2009
荒井保明，竹内義人，稲葉吉隆，新槇 剛	消化器症状の医学的治療 IVR	がん看護	13	279-284	2008
Inaba Y, Arai Y, Aramaki T, et al.	Phase I/II Study of Hepatic Arterial Infusion Chemotherapy With Gemcitabine in Patients With Unresectable Intrahepatic	Am J Clin Oncol	in press		2010
Tokue H, Tsushima Y, Arai Y, et al.	Jejunogastric intussusception: life-threatening complication occuring 55 years after gastrojejunostomy.	Intern Med	48	1657-60	2009

Sofue K, Tateishi U, Arai Y, et al.	Role of carbon-11 choline PET/CT in the management of uterine carcinoma: initial experience.	Ann Nucl Med	23	235-43	2009
Hirokawa T, Sawai H, Arai Y, et al.	Middle-colic artery aneurysm associated with segmental arterial mediolysis, successfully managed by transcatheter	Surg Today.	39	144-7	2009
Kobayashi T, Arai Y, Takeuchi Y, et al	Phase I/II I/II clinical study of percutaneous vertebroplasty (PVP) as palliation for painful malignant	Ann Oncol.	20	1943-7	2009
Tokuda T, Tanigawa N, Kariya S, et al.	Pancreatitis after transcatheter embolization of a splenic aneurysm.	Jpn J Radiol	28	239-42	2010
Suzuki S, Tanigawa N, Kariya S, et al.	Posterior Reversible Encephalopathy Syndrome Occurring After Uterine Artery Embolization for Uterine Myoma.	Cardiovasc Intervent Radiol	In press		2010
Kashima M, Yamakado K, Tanigawa N, et al.	Radiofrequency ablation for the treatment of bone metastases from hepatocellular carcinoma.	AJR Am J Roentgenol	194	536-41	2010
Tokuda T, Tanigawa N, Shomura Y, et al.	Transcatheter embolization for peripheral pseudoaneurysms with n-butyl cyanoacrylate.	Minim Invasive Ther Allied	18	361-5	2009
Tanigawa N, Kariya S, Komemushi A, et al.	Cement leakage in percutaneous vertebroplasty for osteoporotic compression fractures with or without	AJR Am J Roentgenol	193	W442-5	2009
Tokuda T, Tanigawa N, Shomura Y, et al.	Transcatheter embolization for peripheral pseudoaneurysms with n-butyl cyanoacrylate.	Minim Invasive Ther Allied	1	1-5	2009
Satoi S, Yanagimoto H, Tanigawa N, et al.	Pre-operative patient selection of pancreatic cancer patients by multi-detector row CT.	Hepatogastroenterology	56	529-34	2009
Tokuda T, Shomura Y, Tanigawa N, et al.	Mechanical characteristics of composite knitted stents.	Cardiovasc Intervent Radiol	32	1028-32	2009
Kariya S, Tanigawa N, Kojima H, et al.	Percutaneous translumbar inferior vena cava cannulation under computed tomography guidance.	Jpn J Radiol	27	176-9	2009

Kariya S, Tanigawa N, Kojima H, et al.	Peripheral stent placement in hemodialysis grafts.	Cardiovasc Intervent Radiol	32	960-6	2009
Satoi S, Yanagimoto H, Tanigawa N, et al.	Surgical results after preoperative chemoradiation therapy for patients with pancreatic cancer.	Pancreas	38	282-8	2009
Tanigawa N, Kariya S, Kojima H, et al.	Transcatheter coil embolization of an aneurysm of an anomalous splenic artery: usefulness of double microcatheter	Minim Invasive Ther Allied	18	311-4	2009
Kojima H, Tanigawa N, Kariya S, et al.	High-flow priapism undergoing arterial embolization: review of literature following American Urological	Minim Invasive Ther Allied	18	1-5	2009
Takizawa K, Shimamoto H, Nakajima Y, et al.	Development of a new subclavian arterial infusion chemotherapy method for locally or recurrent advanced breast cancer using	Cardiovasc Intervent Radiol.	32	1059-66	2009
Suenaga M, Mizunuma N, Matsueda K, et al.	Management of venous thromboembolism in colorectal cancer patients treated with bevacizumab.	Med Oncol	In press		2009
Shitara K, Matsuo K, Inaba Y, et al.	Neutropaenia as a prognostic factor in metastatic colorectal cancer patients undergoing chemotherapy with first-line	Eur J Cancer.	45	1757-63	2009
Tanigawa N, Kariya S, Kojima H, et al.	Cerebral microembolization during radiofrequency ablation of lung tumors: Detection by carotid duplex	Br J Radiol.	82(975)	249-253	2009
Kariya S, Tanigawa N, Kojima H, et al.	Transcatheter Coil Embolization of Collateral Veins for Steal Syndrome Associated with Hemodialysis Access	Acta Radiologica	50(1)	28-33	2009
Tanigawa N, Kariya S, Komemushi A, Tokuda T, Nakatani M, Yagi	Cement leakage in percutaneous vertebroplasty for osteoporotic compression fracture with or without	Am J Roentgenol	193(5)	442-445	2009
Shomura Y, Tanigawa N, Tokuda T, Kariya S, Kojima H,	Composite material stent comprising metallic wire and Poly Lactic Acid fibers, and its mechanical strength and	Acta Radiol	50(4)	355-359	2009
Tenjin H, Mandai A, Tanigawa N, et al	Percutaneous vertebroplasty using three-dimensional radiography	Neurol Med Chir (Tokyo)	49(4)	179-183	2009

Yukisawa S, Matsueda K, et al.	Upper-extremity deep vein thrombosis related to central venous port systems implanted in cancer patients.	EJR		Epub ahead of print	2010
Suenaga N, Matsueda K, et al.	Management of venous thromboembolism in colorectal cancer patients treated with bevacizumab.	Med Oncol.		Epub ahead of print	2009
松枝　清	消化管出血に対する内視鏡以外の診断・治療法の最近の進歩	臨床消化器内科	24(8)	1153-1162	2009
Akiyoshi T, Matsueda K, et al.	Comparison of preoperative whole-body positron emission tomography with MDCT in patients with primary colorectal cancer.	Colorectal disease	11(5)	464-469	2009
佐藤信吾,松枝　清,ほか	仙骨骨巨細胞腫に対する動脈塞栓術	関節外科	28(6)	713-718	2009
Matsumoto K, Inaba Y, et al	Ruptured pseudoaneurysm of the splenic artery complicating endoscopic ultrasound-guided fine-needle aspiration	Endoscopy.	42	E27-E28	2010
山浦秀和、稲葉吉隆、他	集学的治療における肝動注化学療法の位置づけ	外科	72	153-157	2010
Kobayashi T, Arai Y, Takeuchi Y, Inaba Y, et al	Phase I/II clinical study of percutaneous vertebroplasty (PVP) as palliation for painful malignant vertebral compression	Ann Oncol.	20	1943-1947	2009
Kanemitsu Y, Inaba Y, et al	A randomized phase II/III trial comparing hepatectomy followed by mFOLFOX6 with hepatectomy alone as treatment for liver	Jpn J Clin Oncol.	39	406-409	2009
名嶋弥菜、稲葉吉隆、他	肝動脈化学塞栓療法のエビデンス	腫瘍内科	4	307-312	2009

III. 研究成果の刊行物・別刷

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CLINICAL INVESTIGATION

Hepatic Arterial Infusion Chemotherapy through a Port-Catheter System as Preoperative Initial Therapy in Patients with Advanced Liver Dysfunction due to Synchronous and Unresectable Liver Metastases from Colorectal Cancer

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Abstract
Purpose We retrospectively evaluated the safety and efficacy of preoperative initial hepatic arterial infusion chemotherapy (HAIC) through a port-catheter system in patients with liver dysfunction due to synchronous and unresectable liver metastases. The aim of HAIC was to improve patients' clinical condition for later surgical removal of primary colorectal cancer.
Methods Port-catheter systems were placed radiologically in 21 patients (mean age 58.6 ± 8.1 years) with liver dysfunction due to synchronous liver metastases from colorectal cancer. Initial HAIC of 1,000 mg/m^2 5-fluorouracil was administered weekly as a 5 hr continuous infusion through this system. Surgical removal of the primary lesion was planned after HAIC improved the liver function.
Results Port-catheter system placement was successful in all patients without severe complications. Patients were followed up for a median of 309 days (range 51–998 days). After starting HAIC, no severe adverse events that caused drug loss and treatment postponement or suspension were observed in any of the patients. HAIC was performed a mean of 4.5 ± 3.0 times and the liver function improved in all patients. Curative (n = 18) or palliative (n = 1) surgical removal of the primary lesion was performed. The remaining 2 patients died because extrahepatic metastases developed and their performance status worsened; thus, surgery could not be performed. The median survival times of all patients and the operated patients were 309 and 386 days, respectively.
Conclusion Initial HAIC administration is a safe and efficacious method for improving liver function prior to operative resection of primary colorectal cancer in patients with liver dysfunction due to synchronous and unresectable liver metastases.

Keywords Colorectal cancer · Hepatic arterial infusion chemotherapy · Liver metastasis · Port-catheter system

Introduction

Colorectal cancer is the fourth most commonly diagnosed malignant disease worldwide [1], and synchronous liver metastases are identified in 10–20% of cases [2]. However, the treatment protocol for patients with stage IV colorectal cancer with synchronous liver metastases has not been firmly established [2, 3]. In such patients, the choice of treatment strategy differs based on various factors such as liver function, the patient's condition, the urgency of operating on the primary lesion, and the institution's protocols for dealing with liver metastases and primary lesions. For the primary lesion, it is desirable that surgical removal is selected to improve the quality of life of the patients, because colorectal cancer may cause obstruction, perforation, bleeding, or pain [3]. Additionally it has been reported that stage IV patients who underwent resection of their asymptomatic primary lesions had prolonged median and 2-year survival periods compared with stage IV

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patients who did not undergo resection [3]. However, patients with advanced liver dysfunction due to synchronous liver metastases are not good candidates for surgical removal of the primary lesion. In such circumstances, surgeons and anesthetists usually hesitate to perform surgical removal of the primary lesion, mainly because the patient's condition is too poor to perform surgery and the liver is seen to be the prognosis-limiting factor. As a result insufficient and palliative systemic chemotherapy might be selected without performing surgical removal of the primary lesion in many cases.

With the recent advances in interventional radiology techniques, radiological placements of port-catheter system are increasingly being used in Japan [4, 5]. Repeated hepatic arterial infusion chemotherapy (HAIC) that is performed through an implanted port-catheter system is an effective therapy employed for unresectable advanced liver malignancies [6–8]. In particular, many reports have indicated that HAIC is effective for liver metastases from colorectal cancer [6–8]. It reported that, compared with systemic chemotherapy, HAIC increased the possibility of tumor response and might improve liver function [6].

The purpose of this study was to retrospectively evaluate the safety and efficacy of the initial administration of HAIC through a port-catheter system in patients with advanced liver dysfunction due to synchronous and unresectable liver metastases from colorectal cancer. The aim of HAIC was to improve their clinical condition for the later surgical removal of the primary lesion.

Materials and Methods

Approval from the institutional review board of our hospital and informed consent from all the patients were obtained before performing any procedure.

Patients

Between January 2000 and October 2004, 212 patients with unresectable liver metastases from colorectal cancer underwent radiological placement of port-catheter systems at our institution. In this study, 21 of 212 patients (4 men, 17 women; age 39–77 years, mean 58.6 ± 8.1 years) initially received HAIC through this system to prepare for the surgical removal of the primary lesion later; these patients had liver dysfunction due to synchronous liver metastases. The primary sites of malignancy were as follows: the cecum ($n = 2$), ascending colon ($n = 5$), transverse colon ($n = 3$), sigmoid colon ($n = 7$), and rectum ($n = 4$). With the exception of 1 patient who had a large metastasis in the right lobe of the liver, all patients had diffuse or multiple metastases in both the right and left lobes of the liver. All hepatic lesions were unresectable. All patients had advanced liver dysfunction due to liver metastases, with increased levels of aspartate aminotransferase (AST; mean 110 ± 109 IU/l, range 21–549 IU/l), alanine aminotransferase (ALT; mean 59 ± 43 IU/l, range 17–183 IU/l), total bilirubin (T-BIL; mean 1.0 ± 0.5 mg/dl, range 0.3–2.2 mg/dl), lactate dehydrogenase (LDH; mean 1242 ± 1002 IU/l, range 221–3,870 IU/l), alkaline phosphatase (ALP; mean 874 ± 570 IU/l, range 416–2660 IU/l), and gamma-glutamyl transpeptidase (GTP; mean 393 ± 433 IU/l, range 130–2,023 IU/l). Since the liver dysfunction in these patients had already progressed, we decided to initially administer HAIC instead of the standard systemic chemotherapy in order to improve their liver function. Even in patients with extrahepatic metastases, we initially administered HAIC because we judged that liver metastasis was the prognosis-limiting factor. In 6 of 21 patients, extrahepatic metastases were observed in organs such as the lung ($n = 5$), bone ($n = 1$), and lymph nodes ($n = 1$). Only 1 patient showed evidence of hepatitis B and C virus infection; no other patient had a history of hepatitis. Usually, we consider T-BIL levels >3.0 mg/dl or an Eastern Co-operative Oncology Group performance status [9] of 4 as the exclusion criteria for HAIC administration. However, in this retrospective study, despite conforming to the exclusion criteria, 4 of 212 patients underwent HAIC; these patients were not included in the analysis because these were not planned surgeries.

Port-Catheter System Placement and HAIC

All procedures for the placement of port-catheter systems were performed by interventional radiologists in the angiography suite with the patients under local anesthesia. The procedure was performed as follows. All patients underwent angiography before catheter placement, which was performed using a 5 Fr angiographic catheter (Clinical Supply, Gifu, Japan) inserted from the right femoral artery to allow arterial mapping and to prevent extrahepatic influx of the anticancer agents. The extrahepatic arteries branching from the hepatic artery, such as the right gastric artery, posterior superior pancreatoduodenal artery, and superior duodenal artery, were embolized with microcoils (Tornado; Cook, Bloomington, IN, USA or Trufill; Cordis, Miami Lakes, FL, USA) through a 2.5 Fr microcatheter (Jamiro; Kaneka, Osaka, Japan or Sniper; Clinical Supply, Gifu, Japan) inserted coaxially [10, 11]. In patients with more than two hepatic arteries, these arteries were converted into a single arterial supply by microcoil embolization so that drugs could be distributed to the entire liver using a single indwelling catheter [10]. Next, a 5 Fr angiographic catheter

was inserted from the left subclavian artery and advanced to the common hepatic artery via the celiac artery. Then an indwelling catheter (Anthron P-U catheter; Toray Medical, Tokyo, Japan or W spiral catheter; PIOLAX, Yokohama, Japan) with a side hole was inserted using the catheter-exchange method. The catheter tip was inserted into the deep segment of the gastroduodenal artery so that the side hole was placed into the common hepatic artery. The gastroduodenal artery around the tip of the indwelling catheter was embolized using microcoils and a mixture (1:1.5) of *n*-butyl cyanoacrylate (NBCA; Histoacryl; Braun, Melsungen, Germany) and iodized oil (Lipiodol Ultrafluide; Laboratoire Guerbet, Roissy, France) through a microcatheter inserted coaxially via the 5 Fr angiographic catheter inserted from the right femoral artery. Finally, the proximal end of the indwelling catheter was connected to a port implanted in the subcutaneous pocket created in the left chest wall.

Digital subtraction angiography and CT were performed during injection of contrast medium through the implanted port-catheter system within a few days of implantation to confirm that the catheter was not dislodged and that the entire liver was perfused adequately. Thereafter, HAIC was administered through this system: 1,000 mg/m^2 of 5-fluorouracil (5-FU) weekly by continuous 5 hr infusion [7]. After administration of the chemotherapeutic agent, the implanted port-catheter system was flushed and filled with 2 ml of heparin solution (1,000 IU/ml).

Statistical Analysis

The success rate and the complications of the placement of the port-catheter system were evaluated. After starting HAIC the clinical course, including improvement in liver function tests, performance of surgery, and survival were evaluated. In patients who underwent surgical removal of the primary lesion, the frequency of HAIC administration, time between the placement of the port-catheter system and surgery, details of the surgery, postoperative therapy, and survival were evaluated. The Wilcoxon signed rank test was used to compare the liver functions before surgery with those before starting HAIC. The cumulative survival rate was calculated using the Kaplan-Meier method.

A p value of less than .05 was considered significant.

Results

After placement of the port-catheter system, patients were followed up for a median of 309 days (range 51–998 days).

Placement of the Port-Catheter System

The radiological placement of the port-catheter system was successful in all 21 patients. During and after the procedure, there were no complications such as hematoma, subclavian or vertebral artery thrombosis, infections, hepatic artery occlusions, and catheter malfunctions.

Clinical Course after Starting HAIC

After starting HAIC, no severe adverse events that caused drug loss and treatment postponement or suspension were observed in any of the patients. HAIC was performed a mean of 4.5 ± 3.0 times (range 1–15 times) and the liver function improved in all 21 patients. In particular, the AST, ALT, LDH, ALP, and GTP levels were improved significantly (Table 1). In 19 of 21 patients, curative (n = 18) or palliative (n = 1) surgical removal of the primary lesion was performed. In the remaining 2 patients, although the liver function had improved after HAIC was administered 15 times and 5 times, respectively, extrahepatic metastases in the lung, bone or peritoneum developed rapidly and their performance status worsened. Though systemic chemotherapy was administered with or instead of HAIC afterward, they died 186 and 51 days, respectively, after the placement of port-catheter system; thus, surgery could not be performed.

Among the 19 patients who underwent surgery, HAIC was administered a mean of 3.9 ± 1.8 times (range 1–9 times), and the median period between placement of the

Table 1 Liver function before and after HAIC administration

		Before starting HAIC	After HAIC	p value
AST (IU/l)	Mean	110 ± 109	56 ± 55	
	Range	21–549	21–273	0.0001*
ALT (IU/l)	Mean	59 ± 43	31 ± 22	
	Range	17–183	11–101	0.0005*
T-BIL (mg/dl)	Mean	1.0 ± 0.5	1.2 ± 1.1	
	Range	0.3–2.2	0.3–4.4	0.717
LDH (IU/l)	Mean	1242 ± 1002	551 ± 501	
	Range	221–3870	174–2050	<0.0001*
ALP (IU/l)	Mean	874 ± 570	663 ± 526	
	Range	416–2660	124–2335	0.0046*
GTP (IU/l)	Mean	393 ± 433	207 ± 169	
	Range	130–2023	9–602	0.0061*

AST, aspartate aminotransferase; ALT, alanine aminotransferase; T-BIL, total bilirubin; LDH, lactate dehydrogenase; ALP, alkaline phosphatase; GTP, gamma-glutamyl transpeptidase; HAIC, hepatic arterial infusion chemotherapy

*Significant at $p < 0.05$

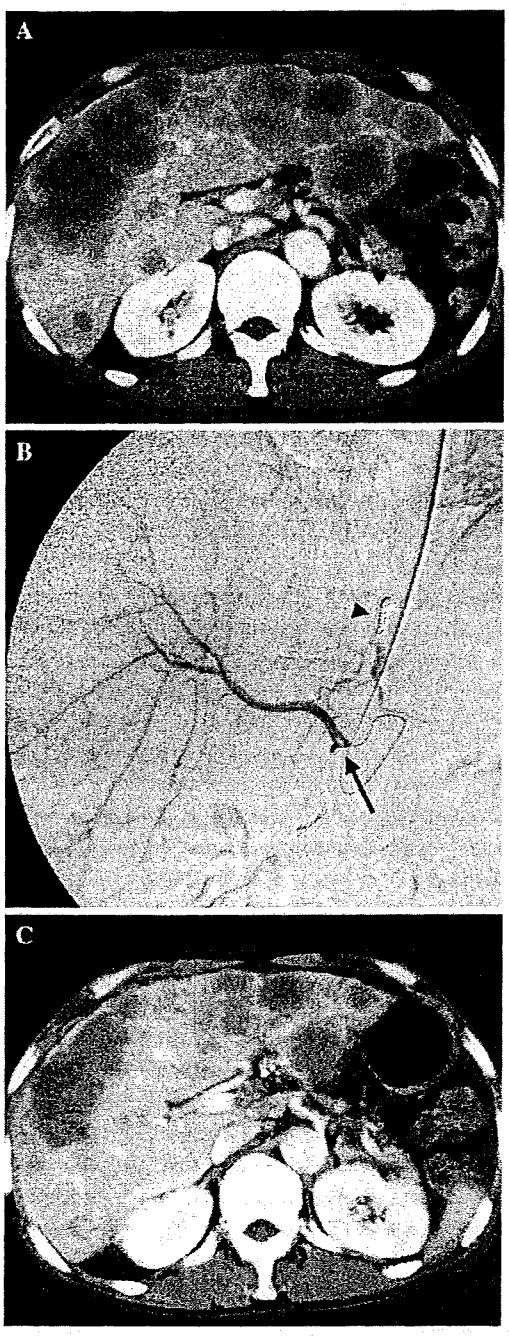

Fig. 2 A–C. A 55-year-old man with multiple liver metastases from rectal cancer. **A** Contrast-enhanced CT scan obtained before starting HAIC shows unresectable multiple liver metastases in both the right and left lobes. **B** An arteriogram via the port obtained before starting HAIC shows that all hepatic arteries are well visualized. The catheter tip was inserted into the deep segment of the gastroduodenal artery and embolized using microcoils and a mixture of *n*-butyl cyanoacrylate and iodized oil. The side hole was placed into the common hepatic artery (arrow). The accessory left hepatic artery, which branched from the left gastric artery, was embolized with microcoils (arrowhead) in order to establish hepatic arterial supply from a single vessel. **C** Contrast-enhanced CT scan obtained after five HAIC administrations shows slightly smaller multiple liver metastases. With the exception of T-BIL, the patient's liver function improved (AST improved from 83 to 26 IU/l, ALT improved from 49 to 18 IU/l, LDH improved from 1,155 to 458 IU/l, and ALP improved from 950 to 502 IU/l)

port-catheter system and surgery was 29 days (range 14–68 days). Of 13 patients who had no extrahepatic metastases prior to the surgery, 10 developed extrahepatic metastases. Among 16 of 19 patients, systemic chemotherapy with or instead of HAIC was administered after the surgery.

The overall median survival time of all the patients was 309 days and that of the patients who underwent surgery was 386 days (Fig. 1). At present, 20 patients have died.

A representative case is shown in Fig. 2.

Discussion

Many studies have reported the effectiveness of HAIC administration through a port-catheter system for liver metastases from colorectal cancer [6–8]. In Western countries, it has been reported that HAIC is effective in treating liver metastases; however, it does not improve the prognosis [6]. On the other hand, in Japan, good results have been reported after intermittent hepatic arterial infusion of a high dose of 5-FU: the response rate is reportedly 78% and the median survival time is 25.8 months [7].

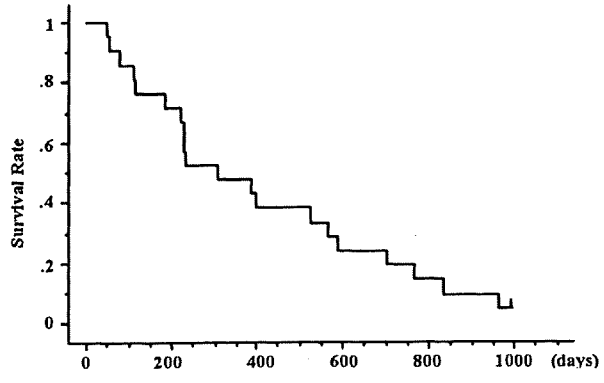

Fig. 1 Overall survival time

In general, systemic chemotherapy is usually selected for colorectal cancer with distant metastases [2]. Recently, the standard regimens such as FOLFILI (5-FU plus leucovorin with oxaliplatin) and FORFOX (5-FU plus leucovorin and irinotecan) are used, and the median survival after FOLFILI and FORFOX has been reported to be 12.6–21.5 months [12]. In many cases, systemic chemotherapy might be the first choice of treatment for patients with primary colorectal cancer and synchronous distant metastases, and we usually select systemic chemotherapy