Q 前頭葉に白い，親指ぐらいのものが写っているのですが，それは「がん」とつながりはあるのでしょうか。

A 脳にできものができれば，それが最終的にがんになる可能性はあるかもしれませんが，いまのご質問の内容だけで，それががんになるかどうかは分かりません。実際にお写真を見せていただいて診察をさせていただかないと，分からないことです。

ご質問からはずれますが，よく聞かれることなので，病気の呼び方について少しお話します。

このがんセンターで扱う病気の多くは「がん」と呼ばれます。胃がんとか，肺がん，乳がんといった具合ですね。ところが本日の話では，僕は「脳腫瘍」という言葉を使って，「脳がん」「脳のがん」とは言っていないのです。私どもは一般的に脳にできた腫瘍を，そう呼んでおりません。「なぜならば…」，と説明できればカッコいいのですが，脳腫瘍研究の歴史に詳しい先生の何人かの方にお話を聞いても，なぜ「脳がん」と呼ばないかの答えが分からないのです。

ただ，脳に，もちろんがんは起こります。以前，この講演会シリーズで整形外科の先生がお話をされたと思いますが，大きく「がん」というのは，からだの中にできる悪性の腫瘍，要するにそのまま放っておいたらどんどん自己増殖して，からだをむしばんで，人間を壊してしまう，そういう腫瘍の総称を平仮名で「がん」と呼ぶわけですね。ですから，骨や筋肉にできる「肉腫」も，胃などの臓器にできる「癌」も，総称して「がん」と平仮名で表記しており，だからがんセンターの「がん」は，その両方の意味で，平仮名で書いてあるわけです。脳にできた腫瘍の中には「がん」と呼べるものはあり，「それは癌か，肉腫か」というと，「肉腫ではなく癌」，ということになります。

Q 原発性脳腫瘍の原因は分からないとお話されましたが，現在研究上でその可能性があると考えられているものはないのでしょうか。

A 実際，私もがんの原因は知りたいところです。お話したように，脳腫瘍が脳卒中や頭部外傷と大きく違うのは，「予防できるか，できないか」ということです。ですから，脳外科医に限らず，がんの治療に当たっている医者は，みんなそれを知りたいのですね。原因が分かれば，その原因をあらかじめさかのぼって封じ込められれば，予防ができるのです。残念ながら，ここで皆

さんにお話しできるような，実際に予防につながるような脳腫瘍の原因というのは，今のところ分かっておりません。

Q 原発性脳腫瘍に対して大変難しい手術をしていただき，マヒもなく退院できる見込みになったことを，まず御礼申し上げます。退院後，一番心配なのは，再発です。手術で治療した後，再発する可能性というのは，数字で出せるのかという点と，今回は右脳の前頭葉だったのですが，なぜここにできたのか，ほかの部位にも同じようにできる可能性があるのかをお教えください。

A 後半の質問からお答えすると，脳腫瘍はどこに起きてもおかしくない病気です。原因はよく分かりませんが，腫瘍になる危険性，可能性は，脳のどこにでもあります。

前半の質問ですが，再発の問題というのは，どの方も心配なところだと思います。再発というのは，それが良性腫瘍であろうが悪性腫瘍であろうが，可能性はやはりゼロではありません。また，悪性という名前がつくぐらいですから，良性腫瘍に比べれば悪性腫瘍のほうが，再発の可能性は高くあります。ですが，良性腫瘍だからといって再発しないわけではありませんし，悪性腫瘍だからといって，必ず早いスピードで再発するというわけでもありません。ですから，「次の外来での検査は，こうしましょう」と言うときは，ただやみくもに検査をしているわけでは決してないのです。ある程度再発する可能性が高い方では，検査の間隔を短くして経過をみますし，良性腫瘍の患者さんであれば，例えば6カ月なり1年なり，長い方では2年に1回という間隔で検査をして，問題はないと考えられる間隔で私どもはスケジュールを組みます。

ただ，再発では，最初に出てきたものと同じような症状が出てくる可能性が高いので，患者さんにはそうした症状にも気をつけていただいて，症状が出れば，そこで検査を行うこともあります。

退院されるということですから，これからそうした詳しいお話があると思います。主治医の先生に直接，よくお話を聞いていただければと思います。

Q 肺がんからの転移性の脳腫瘍ですが，それをガンマナイフで治療した場合，同じ部位を2回はできないと聞いています。それはどういう理由でしょうか。

A 放射線治療に限らず，治療の裏側には副作用と呼ばれる，必ず悪いことがあります。腫瘍がある場所に放射線を当てれば，腫瘍に到達するまでの間の場所にもやはりある程度の放射線が当たります。ですから，脳に限らず，放射線治療は臓器ごとに照射できる絶対量が決められているのです。また，多くの場合，高い治療効果を期待して，最初の治療でその限界までの放射線量を使って治療するのが放射線治療の基本です。その限界の量をできるだけ1カ所に集中するのがガンマナイフという方法です。1回目で限界の量を使っていますから，2回目はできない，もしくは行う場合には副作用の危険が高くなるというのが，その理由です。

Volume 17
Number 1
2005
ISSN 0915-5635

Digestive Endoscopy

Journal for Gastroenterologists and Endoscopic Surgeons

Blackwell Publishing

Official Journal of the Japan Gastroenterological Endoscopy Society and Asian Pacific Society for Digestive Endoscopy

Digestive Endoscopy (2005) **17**, 54–58

ORIGINAL ARTICLE

ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER: TECHNICAL FEASIBILITY, OPERATION TIME AND COMPLICATIONS FROM A LARGE CONSECUTIVE SERIES

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Background: Endoscopic mucosal resection (EMR) is a recognized treatment for early gastric cancer (EGC). One-piece resection is considered to be a gold standard of EMR, as it provides accurate histological assessment and reduces the risk of local recurrence. Endoscopic submucosal dissection (ESD) is a new technique developed to obtain one-piece resection even for large and ulcerative lesions. The present study aims to identify the technical feasibility, operation time and complications from a large consecutive series.

Methods: We reviewed all patients with EGC who underwent ESD using the IT knife at National Cancer Center Hospital in the period between January 2000 and December 2003.

Results: During the study period of 4 years we identified a total of 1033 EGC lesions in 945 consecutive patients who underwent ESD using the IT knife. We found a one-piece resection rate (OPRR) of 98% (1008/1033). Our OPRR with tumor-free margins was 93% (957/1033). On subgroup analysis it was found to be 86% (271/314) among large lesions (≥ 21 mm) and 89% (216/243) among ulcerative lesions. The overall non-evaluable resection rate was 1.8% (19/1033). The median operation time was 60 min (range; 10–540 min). Evidence of immediate bleeding was found in 7%. Delayed bleeding after ESD was seen in 6% and perforation in 4% of the cases. All cases with complications except one were successfully treated by endoscopic treatment.

Conclusion: The present study shows the technical feasibility of ESD, which provides one-piece resections even in large and ulcerative EGC.

Key words: complication, early gastric cancer, endoscopic submucosal dissection, insulation-tipped knife, one-piece resection.

INTRODUCTION

The incidence of early gastric cancer (EGC) varies between countries, reaching 40–60% of cases in Japan.[1–4] Recently, local treatment for EGC by endoscopic mucosal resection (EMR) has been accepted as a standard treatment strategy for selected cases of EGC.[5,6] EMR provides a 5-year survival rate of 85% equivalent to that of surgery and is devoid of traditional surgical morbidity and mortality.[7–9] One-piece resection is considered to be a gold standard of EMR as it provides accurate histological assessment and reduces the risk of local recurrence.[10] The general criteria for EMR in EGC proposed by the Japanese Gastric Cancer Association includes: (i) differentiated adenocarcinoma; (ii) intramucosal cancer; (iii) ≤ 20 mm in size; and (iv) without ulcer finding.[10] Lesions that meet all of the above criteria have negligible risk of lymph node metastasis and have a reasonable tumor size allowing one-piece resection by conventional EMR.[10–14]

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Received 8 April 2004; accepted 5 July 2004.

We proposed expansion of these general criteria for EMR in EGC based on the risks of lymph node metastasis in EGC obtained from a large number of surgical cases.[10,15] The expanded criteria (Table 1) include lesions ≥ 21 mm and ulcerative lesions which were originally resected by surgery. By expanding the criteria for EMR as suggested above the need for gastrectomy in EGC can be reduced, as these patients could be treated by EMR. However, it is difficult to resect large and ulcerative lesions by conventional EMR techniques so a new technique of endoscopic submucosal dissection (ESD) has been developed.[16–20] The primary aim of this technique is to obtain one-piece resection during EMR. It starts with identification and demarcation of the lesion margins, which are then marked with a needle knife. This is followed by submucosal injections at the margins to lift the mucosa and then a circumferential mucosal incision is performed around the lesion. Subsequent submucosal dissection of the lesion is performed with a special knife. We developed an insulation-tipped (IT) knife for ESD in 1996.[17,18] This knife is a modification of traditional needle knife and has an insulated ceramic tip which reduces the risk of gastric wall perforation. Over the years we have gained substantial experience and expertise in the use of this knife and, for last 5 years, ESD with the IT knife has become a

Table 1. Expanded histological criteria of endoscopic submucosal dissection

1. Differentiated adenocarcinama
2. No lymphatic or venous invasion
3. Intramucosal cancer regardless of tumor size without ulcer finding Intramucosal cancer ≤ 30 mm in size with ulcer finding Minute subumucosal cancer (sm1) ≤ 30 mm in size

Table 2. Expanded indication before endoscopic submucosal dissection

1. Differentiated adenocarcinoma
2. No apparent invasive findings to the submucosal layer
3. Regardless of tumor size without ulcer finding ≤ 30 mm in size with ulcer finding

standard practice in the treatment of EGC at our center. In the present study, we aim to review the one-piece resection rate (OPRR), operation time and complications of ESD using the IT knife in the treatment of EGC in a large series of patients. To our knowledge, there is no other reported series of similar size in the literature.

PATIENTS AND METHODS

We perform ESD for EGC that meet the expanded indications before treatment at National Cancer Center Hospital (Table 2) and then curability is determined histopathologically based on the expanded criteria (Table 1) and tumor margins.

We identified all patients with EGC who underwent ESD using the IT knife at our center in the period between January 2000 and December 2003.

We reviewed the clinical records, endoscopic and histological reports of all these patients. A data collection sheet was designed to obtain the relevant demographic and clinical information about the patient, the tumor, the procedure and its complications. Location of the tumor was divided into upper, middle and lower thirds of the stomach based on the Japanese Classification of Gastric Carcinoma.[21] Tumor size and ulcer finding were determined histopathologically. One-piece resection was defined as en bloc resection. Resections were considered to have tumor-free margins when both vertical and horizontal margins of the specimen were free of tumor cells independently of histological features. One-piece resection rate (OPRR) with tumor-free margins was further evaluated according to location, size and ulcer finding. Curability was divided into curative, non-curative and non-evaluable based on the expanded histological criteria (Table 1) and tumor margins.[10,15] Procedure-related bleeding was subdivided into immediate and delayed. Immediate bleeding was estimated in terms of a difference in hemoglobin (Hb) level between preprocedure and next-day Hb value and a decrease of ≥ 2 g/dL in Hb level was defined as significant. Patients with a drop in Hb levels of ≥ 2 g/dL following ESD but with values within normal minimum limit (male 13.7 g/dL, female 11.3 g/dL) were not considered to have had significant blood loss (to allow for hemodilution). Delayed bleeding was defined as clinical evidence of bleeding as evidenced by hematemesis or melena at 0–30 days after the procedure and requiring endoscopic treatment. We also recorded the incidence of perforation as seen during endoscopy or evidenced clinically after the procedure. Procedure-related mortality was defined as any death within 30 days of ESD.

Data were analyzed using the χ^2 test (Statview; Abacus Concepts, Inc., Berkeley, CA, USA). Fisher exact test was used when appropriate and $P < 0.05$ was considered significant.

Table 3. Characteristics of early gastric cancer

Location	U	176 (17%)
	M	431 (42%)
	L	426 (41%)
Size (mm)	≤ 20	719 (70%)
	21–30	176 (17%)
	≥ 31	138 (13%)
Ulcer finding	Positive	243 (24%)
	Negative	790 (76%)

L, lower third; M, middle third; U, upper third.

RESULTS

Clinicopathological features

During the study period of 4 years we identified a total of 1033 EGC lesions in 945 consecutive patients. Median age of the patients was 67 years with a mean age of 66.6 years (range; 29–93 years) and the male/female ratio was 4.20 (764/181). Among 1033 lesions, 30% were ≥ 21 mm and 24% had ulcer finding. Overall data regarding location, tumor size and ulcer finding are described in Table 3.

One-piece resection rate

Among 1033 consecutive lesions resected at our center, one-piece resection was obtained in 1008 lesions (OPRR; 98%). The overall OPRR with tumor-free margins was 93% (957/1033). The relationship between OPRR with tumor-free margins and tumor location, size and ulceration is shown in Table 4.

Curability

Assessment of histological curability is shown in Table 5. Among 857 curative resections, 484 were intramucosal cancers ≤ 20 mm without ulcer findings, 149 were intramucosal cancers ≥ 21 mm without ulcer findings, 159 were intramucosal cancers ≤ 30 mm with ulcer findings and 65 were minute subumucosal cancers (sm1) ≤ 30 mm. Among 157 non-curative resections, 141 were not included in the expanded histological criteria (Table 1) regardless of tumor margins and the remaining 16 lesions met these criteria but showed positive horizontal margin. The overall non-evaluable resection rate was 1.8% (19/1033).

Operation time

Our median operation time was 60 min with a mean time of 78 min (range; 10–540 min). The relationship between operation time and tumor location, size and ulceration is shown in Table 6.

Complications

Mortality

There was no death in this large series of patients (mortality rate: 0%).

Immediate bleeding

Evidence of immediate bleeding was found in 63/945 patients (7%). The relationship between immediate bleeding and tumor location, size and ulceration finding is shown in Table 7.

Delayed bleeding

Delayed bleeding after ESD was seen in 59/945 patients (6%). Of these patients, 76% bled within 24 h and the remaining 24% bled between 2 and 15 days after the procedure. The relationship between the risk of delayed bleeding and tumor location, size and ulceration is shown in Table 8. All cases of bleeding were controlled by endoscopic treatments (hemoclipping and/or electrocoagulation) and did not require any surgical intervention. Blood transfusion was required in only one patient.

Perforation

Gastric wall perforation was found in 35/945 patients (4%). The relationship between risk of perforation and tumor size,

Table 4. Relationship between OPRR with tumor-free margin and lesion location, size and ulcer finding

		OPRR with tumor-free margin	*P* value
Location	U	88% (155/176)	< 0.001
	M	91% (394/431)	< 0.01
	L	96% (408/426)	
Size (mm)	≤ 20	95% (686/719)	
	21–30	90% (158/176)	< 0.01
	≥ 31	82% (113/138)	< 0.001
Ulcer finding	Positive	89% (216/243)	< 0.05
	Negative	94% (741/790)	

L, lower third; M, middle third; OPRR, one-piece resection rate; U, upper third.

Table 7. Relationship between immediate bleeding and lesion location, size and ulcer finding

		Diminution of Hb level (≥ 2 g/dL)†	*P* value
Location	U	8% (14/176)	0.01
	M	8% (35/431)	< 0.005
	L	3% (14/426)	
Size (mm)	≤ 20	4% (32/719)	
	21–30	8% (14/176)	0.065
	≥ 31	12% (17/138)	< 0.001
Ulcer finding	Positive	7% (17/243)	0.504
	Negative	6% (46/790)	

L, lower third; M, middle third; U, upper third.
† Cases of Hb level post endoscopic submucosal dissection showing within normal minimum limit were excluded.

Table 5. Assessment of histological curability

	Curative resection	Non-curative resection	Non-evaluable resection
One-piece resection	84% (842/1008)	15% (150/1008)	1.6% (16/1008)
Piecemeal resection	60% (15/25)	28% (7/25)	12% (3/25)
Total	83% (857/1033)	15% (157/1033)	1.8% (19/1033)

Table 6. Relationship between operation time and lesion location, size and ulcer finding

		Operation time (min)					
		≤ 30	31–60	61–120	≥ 121	Mean	Median
Location	U	13% (22/176)	33% (58/176)	35% (62/176)	19% (34/176)	90	70
	M	16% (71/431)	39% (166/431)	27% (117/431)	18% (77/431)	84	60
	L	27% (114/426)	41% (174/426)	24% (102/426)	8% (36/426)	66	55
Size (mm)	≤ 20	26% (190/719)	40% (291/719)	24% (176/719)	9% (62/719)	64	50
	21–30	8% (14/176)	44% (77/176)	30% (53/176)	18% (32/176)	91	60
	≥ 31	2% (3/138)	22% (30/138)	38% (52/138)	38% (53/138)	134	110
Ulcer finding	Positive	9% (23/243)	37% (91/243)	33% (80/243)	20% (49/243)	91	70
	Negative	23% (184/790)	39% (307/790)	25% (201/790)	12% (98/790)	74	60
Total		20% (207/1033)	39% (398/1033)	27% (281/1033)	14% (147/1033)	78	60

L, lower third; M, middle third; U, upper third.

Table 8. Relationship between delayed bleeding and lesion location, size, ulcer finding and time since procedure

		Delayed bleeding	*P* value
Location	U	1% (1/176)	
	M	6% (27/431)	0.001
	L	6% (31/426)	< 0.001
Size (mm)	≤ 20	5% (35/719)	
	21–30	7% (13/176)	0.1838
	≥ 31	8% (11/138)	0.1385
Ulcer finding	Positive	5% (13/243)	
	Negative	6% (46/790)	0.7811
Time	≤ 24 h	76% (45/59)	
	2–7 days	12% (7/59)	
	8–15 days	12% (7/59)	

L, lower third; M, middle third; U, upper third.

Table 9. Relationship between gastric wall perforation and lesion location, size and ulcer finding

		Perforation	*P* value
Location	U	7% (13/176)	< 0.001
	M	4% (16/431)	< 0.05
	L	1% (6/426)	
Size (mm)	≤ 20	3% (18/719)	
	21–30	3% (6/176)	
	≥ 31	8% (11/138)	0.001
Ulcer finding	Positive	6% (14/243)	< 0.005
	Negative	3% (21/790)	

L, lower third; M, middle third; U, upper third.

location and ulceration is shown in Table 9. All perforations were detected endoscopically during the procedure and no patient had delayed or missed perforation. All perforations were managed endoscopically using endoclips except one patient who needed surgery.

DISCUSSION

Development of new EMR techniques, such as ESD, has revolutionized the management of EGC. It is now possible to treat EGC, including large and ulcerative lesions, by ESD at minimal cost and low morbidity and no mortality, in contrast to surgery. One-piece resection has been proposed as a gold standard of EMR as it helps in accurate histological assessment and reduces the risk of tumor recurrence.[10] ESD is a technique developed with the primary aim of obtaining one-piece resection even in large and ulcerative lesions.[16–20]

We have found an OPRR of 98% in our large series of EGC which comprised large ≥ 21 mm (30%) and ulcerative lesions (24%) treated by ESD using IT knife. We believe that this is a significant improvement as compared to an OPRR of 76% with conventional EMR techniques in EGC of smaller size and no ulceration as reported in a review of Japanese literature.[22] This high rate of OPRR led to a very low rate of histologically non-evaluable resection rate of 1.8%. This is again a big improvement as compared to the conventional methods. This ability to assess the histological curability of resection has major therapeutic implications in terms of deciding the need for further treatment.

The ability to obtain resections with tumor-free margins is another big advantage of ESD with the IT knife as evidenced in our series at 93%. On further analysis, we found that OPRR with tumor-free margins is dependent on the location, size and presence or absence of ulceration in the tumor. Lesions ≥ 31 mm, with ulceration and located in the upper third of the stomach have a low rate of obtaining tumor-free resection margins with ESD (Table 4). However, this rate is still higher then that described with conventional EMR techniques and, in our opinion, ESD should be the preferred mode of treatment for such lesions. We believe that tumors with above-mentioned characteristics are technically difficult to resect and should only be performed by endoscopists with a high level of expertise and experience.

In contrast, among 857 curative resections, the number of lesions not included in the general criteria proposed by the Japanese Gastric Cancer Association but included in our expanded criteria reached up to 44% (373/857).

The median operation time in our series was 1 h. On subgroup analysis we found that the operation time was longer in technically difficult lesions as described above (Table 6). We have a large number of trainees operating under guidance and we believe that this would influence the operation time adversely. There is also an issue of the learning curve with this relatively new technique.

One of the anxieties related to the use of the IT knife and performing ESD in technically difficult lesions for a prolonged duration of time is the risk of complications. In our series we found that immediate bleeding was seen in 7% of cases. This is a reflection of intraoperative bleeding and was measured as the difference in Hb levels measured before and the morning after the procedure. This led to inclusion of eight patients who had delayed bleeding within 12 h and a drop in their Hb by ≥ 2 g/dL (data not shown), so this figure is an overestimate of the real incidence of intraoperative bleeding. The intraoperative blood loss seen in these patients was not associated with any hemodynamic changes and none of these patients needed blood transfusion.

The risk of delayed bleeding was seen in 6% of our cases. In all these patients, bleeding was controlled by endoscopic treatment with no need for surgical intervention. Blood transfusion was required in only one patient. This indicates that the delayed bleeding did not have significant hemodynamic consequences. This could be a reflection of our policy of high clinical suspicion and early endscopic intervention in suspected cases of delayed bleeding.

The gastric wall perforation rate observed in our series was 4% and all these perforations were diagnosed at the time of procedure and treated endoscopically. In one patient in whom the perforation was diagnosed at the time of ESD, we could not seal endoscopically due to a technically difficult lesion near the anastmotic site of previous Billroth-1 gastrectomy.

On further analysis we found that the risk of intraoperative bleeding and perforation was again higher in technically difficult cases, but delayed bleeding was common in lesions of the middle and lower third of the stomach. The reason for the latter remains unclear but antral peristaltic activity may contribute to this to some extent. We also believe that this increase in the risk of bleeding from lesions of the lower third

of the stomach could be due to the fact that intraoperative bleeding in this group of lesions is low, thus needing less intraoperative hemostatic treatment as compared to the vessels in the lesions of the upper third of the stomach. This lack of intraoperative intervention may contribute towards the risk of delayed bleeding. We are currently evaluating our data to address this issue.

We conclude that this technique of ESD with the IT knife is a feasible method of treating EGC and has a big advantage of obtaining one-piece resection even in large or ulcerative lesions. There was no procedure-related mortality and there was an acceptable rate of complications that could be managed endoscopically. This has helped us to expand our indications for EMR and reduce the need for surgery in EGC. We are currently collecting long-term outcome data from this large series of patients.

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Jpn J Clin Oncol 2004;34(1)14–19

Radical Cystectomy for Invasive Bladder Cancer: Results of Multi-institutional Pooled Analysis

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Received October 28, 2003; accepted December 7, 2003

Background: We report the outcome of radical cystectomy for patients with invasive bladder cancer, who did not have regional lymph node or distant metastases, at 21 hospitals.
Methods: Retrospective, non-randomized, multi-institutional pooled data were analyzed to evaluate outcomes of patients who received radical cystectomy. Between 1991 and 1995, 518 patients with invasive bladder cancer were treated with radical cystectomy at 21 hospitals. Of these, 250 patients (48.3%) received some type of neoadjuvant and/or adjuvant therapy depending on the treatment policy of each hospital.
Results: The median follow-up period was 4.4 years, ranging from 0.1 to 11.4 years. The 5-year overall survival rate was 58% for all 518 patients. The 5-year overall survival rates for patients with clinical T2N0M0, T3N0M0 and T4N0M0 were 67%, 52% and 38%, respectively. The patients with pT1 or lower stage, pT2, pT3 and pT4 disease without lymph node metastasis had 5-year overall survivals of 81%, 74%, 47% and 38%, respectively. The patients who were node positive had the worst prognosis, with a 30% overall survival rate at 5 years. Neoadjuvant or adjuvant chemotherapy did not provide a significant survival advantage, although adjuvant chemotherapy improved the 5-year overall survival in patients with pathologically proven lymph node metastasis.
Conclusions: The current retrospective study showed that radical cystectomy provided an overall survival equivalent to studies reported previously, but surgery alone had no more potential to prolong survival of patients with invasive cancer. Therefore, a large-scale randomized study on adjuvant treatment as well as development of new strategies will be needed to improve the outcome for patients with invasive bladder cancer.

Key words: multi-institutional pooled analysis – radical cystectomy – invasive bladder cancer

INTRODUCTION

Radical cystectomy has been considered the standard curative treatment for invasive bladder cancer all over the world (1,2). Recent improved surgical techniques in addition to development of perioperative care and anesthesia have reduced morbidity and mortality. Furthermore, advances in orthotopic urinary tract reconstruction have improved the quality of life of

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patients undergoing radical cystectomy. However, while about half of patients are cured, the remainder still suffer from local recurrence and distant metastasis within 2–3 years. Thus, in an attempt to improve treatment outcome, many investigators have tried combinations of neoadjuvant or adjuvant chemotherapy with surgery (3–5). Unfortunately, the impact of neoadjuvant or adjuvant chemotherapy on survival remains controversial. Recently, the South Western Oncology Group (SWOG) showed an improvement in overall survival with three cycles of neoadjuvant chemotherapy consisting of methotrexate, vinblastine, doxorubicin and cisplatin (MVAC) (6). Furthermore, more recent meta-analysis demonstrated that neoadjuvant chemotherapy provided a significant survival advantage in patients with invasive bladder cancer (7).

In this study, we evaluate outcomes of patients with invasive bladder cancer who underwent radical cystectomy with/without pelvic lymph node dissection in 21 hospitals.

PATIENTS AND METHODS

This study included 518 patients with clinically invasive bladder cancer without regional lymph node or distant metastases (T2–4N0M0). All were treated with radical cystectomy with/without pelvic lymph node dissection at 21 hospitals between 1991 and 1995. Using these data, non-randomized, multi-institutional pooled data were analyzed to evaluate the treatment results of radical cystectomy. Tumors were staged according to the criteria of the 3rd edition of General Rules for Clinical and Pathological Studies on Bladder Cancer of the Japanese Urological Association and Japanese Society of Pathology (8). Urothelial carcinoma was the predominant histological type in all patients. Patients with pure squamous cell carcinoma and adenocarcinoma were excluded from this study. Because the pathology of surgical specimens was not reviewed by central pathologist(s), tumor grade was not included in this analysis.

Almost half of the patients received some type of neoadjuvant and/or adjuvant therapy. The type and dose of the additional therapy depended on each institution's preference.

The overall survival was calculated from the date of operation to death from any cause. The overall survival rate was calculated by the Kaplan–Meier method. The statistical significance of differences was determined by the log-rank test. Spearman's rank correlation test was used to analyze correlations between two factors. A P-value of <0.05 was considered statistically significant. All analyses were performed using StatView 5.0 for Macintosh (SAS Institute, NC, USA).

RESULTS

PATIENT CHARACTERISTICS

Patient characteristics are shown in Table 1. More than two-thirds of the patients were male. The mean age at operation was 65.4 years (range, 33–87 years). Half of the patients had a clinical stage of T2N0M0. Pathological examination revealed that patients with pT2 and pT3 accounted for almost 60% of the total, followed by those with pT1 and lower stages and those with pT4. Nearly 90% of patients received lymph node dissection. Lymph node metastasis was histopathologically proven in 86 patients (16.6%), who accounted for 18.4% of those who received node dissection (Table 2). Its incidence was significantly linked with clinical stage ($P < 0.01$ by Spearman's rank correlation test). The incidence clearly increased with progression of the pathological stage from 5.9% in patients with superficial cancer to 32.5% of those with pT4 ($P < 0.01$ by Spearman's rank correlation test).

Table 1. Patient characteristics

Characteristics		No. of patients (%)
Gender	Male	400 (77.2)
	Female	118 (22.8)
Age (years)	33–87 (mean: 65.4)	
Clinical T classification	T2	271 (52.3)
	T3	178 (34.4)
	T4	69 (13.3)
Pathological T classification	≤pT1	119 (23.0)
	pT2	156 (30.2)
	pT3	152 (29.4)
	pT4	90 (17.4)
Lymph node metastasis	pNx	53 (10.2)
	pN0	379 (73.2)
	≥pN1	86 (16.6)
Additional therapy	No	268 (51.7)
	Yes	250 (48.3)
Type of additional therapy	Neoadjuvant	118 (47.2)
	Adjuvant	85 (34.0)
	Neoadjuvant and adjuvant	47 (18.8)

Neoadjuvant and/or adjuvant therapies were performed for 48.3% of 518 patients together with radical cystectomy (Table 3). Of these, 118 patients (47.2%) received some type of therapy in the neoadjuvant setting. These included systemic chemotherapy for 80 patients, intraarterial chemotherapy for 32, radiation for one and combined systemic chemotherapy and local radiation for five. Among the systemic chemotherapies, MVAC, the most popular regimen for urothelial cancer (9), was frequently used. In the adjuvant setting, systemic chemotherapy was administered most frequently. More than half of the patients received MVAC chemotherapy.

OUTCOME

The follow-up period ranged from 0.1 to 11.4 years with a median of 4.4 years. The 5-year overall survival rate was 58% for all 518 patients (Fig. 1), 67% for patients with clinical T2N0M0, 52% for those with T3N0M0 and 38% for those with T4N0M0 (Fig. 2). According to pathological stage, the 5-year

Table 2. Relationships among clinical stage, pathological stage and lymph node metastasis

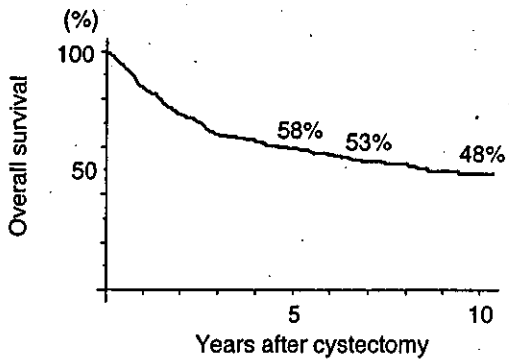
Clinical stage	Pathological stage	No. of patients with radical cystectomy	No. of pathologically node positive patients/no. of patients with node dissection (%)
T2	pT0	26	1/24 (4.1)
	≤pT1	54	4/48 (8.3)
	pT2	110	8/101 (7.9)
	pT3	57	20/53 (37.7)
	pT4	23	6/19 (31.5)
	All	270	39/245 (15.9)
T3	pT0	7	0/4 (0)
	≤pT1	23	2/18 (11.1)
	pT2	41	2/36 (5.5)
	pT3	78	15/71 (21.1)
	pT4	29	9/28 (32.1)
	All	178	28/157 (17.8)
T4	pT0	5	0/5 (0)
	≤pT1	4	0/3 (0)
	pT2	5	2/5 (40.0)
	pT3	17	5/16 (31.2)
	pT4	38	12/36 (33.3)
	All	69	19/65 (29.2)
T2–4	≤pT1	119	7/119 (5.9)
	pT2	156	12/142 (8.4)
	pT3	152	40/140 (28.5)
	pT4	90	27/83 (32.5)

$P < 0.01$ (Spearman's rank correlation test).

Table 3. Type of additional therapy

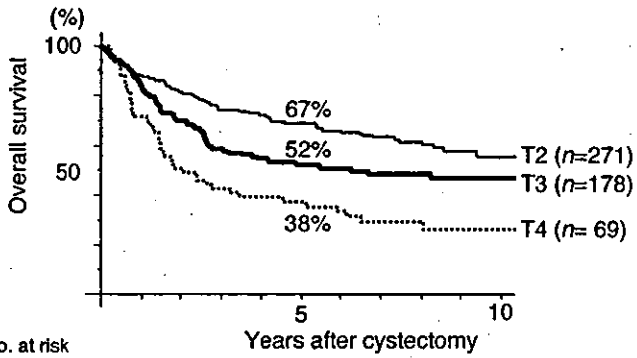
Type		No. of courses (median)	No. of patients
Neoadjuvant			118
Systemic chemotherapy	MVAC*	1–4 (2)	49
	MEC*	1–4 (2)	13
	CDDP-based chemotherapy	1–2 (2)	18
Local therapy	Intraarterial chemotherapy (CDDP-based)	1–2 (1)	32
	Radiation only		1
Systemic and local therapy	Chemotherapy and radiation		5
Adjuvant			85
Systemic chemotherapy	MVAC	1–4 (2)	48
	CISCA*	1–3 (2)	5
	MEC	1–2 (2)	4
	CDDP-based chemotherapy	1–6 (2)	24
	Others		4
Neoadjuvant and adjuvant			47
Intraarterial→systemic			13
Systemic and radiation→systemic			4
Systemic→systemic			30

*MVAC, methotrexate, vincristine, doxorubicin and cisplatin, (21); MEC, methotrexate, epirubicin and cisplatin, (22); CISCA, cisplatin, cyclophosphamide and doxorubicin.



No. at risk 518 411 348 295 272 242 207 148 99 54 29

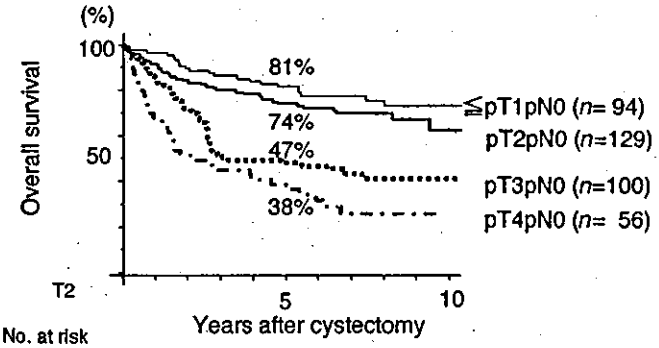
Figure 1. Overall survival rate in all 518 patients.



No. at risk

T2	271	229	207	184	172	153	132	94	60	32	20
T3	178	137	109	85	78	70	59	41	30	16	7
T4	69	45	32	26	22	19	16	12	9	5	2

Figure 2. Overall survival rate according to clinical stage. T2 versus T3, $P < 0.01$; T2 versus T4, $P < 0.001$; T3 versus T3, $P < 0.01$ (log-rank test).

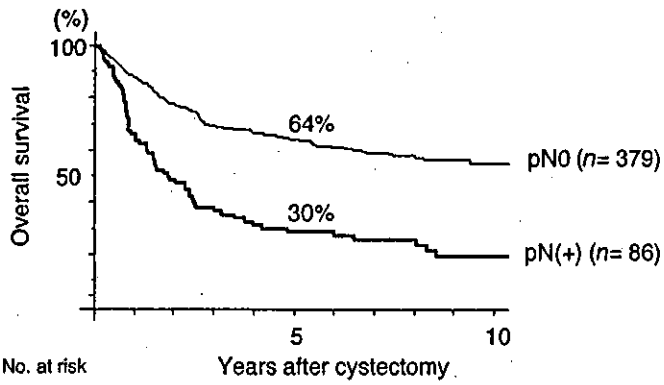


No. at risk

≦pT1pN0	94	88	79	71	69	65	56	45	30	15	9
pT2pN0	129	116	105	100	93	80	72	48	29	16	9
pT3pN0	100	82	67	47	43	39	35	22	12	6	4
pT4pN0	56	33	25	21	19	17	12	6	5	3	0

Figure 3. Overall survival rate according to pathological stage. ≦pT1pN0 versus pT3pN0, pT4pN0, $P < 0.001$; pT2pN0 versus pT3pN0, pT4pN0, $P < 0.001$; pT3pN0 versus pT4pN0, $P = 0.02$ (log-rank test).

overall survival rate was significantly higher for patients with pT1 or a lower stage, or pT2 than for those with pT3 or pT4 disease, when those who were pathologically node negative were considered (Fig. 3). Patients who were pathologically proven to be node positive clearly had a lower 5-year overall survival rate (30%) than those who were node negative (Fig. 4, $P < 0.001$ by log-rank test).



No. at risk

pN0	379	319	276	239	224	201	175	122	76	40	22
pN(+)	86	53	37	29	23	20	18	14	13	8	3

Figure 4. Overall survival rate according to lymph node metastasis. pN0 versus pN(+), $P < 0.001$ (log-rank test).

Impact of Additional Therapy

When we evaluated whether neoadjuvant chemotherapy could improve survival, there was no significant difference with regard to the 5-year overall survival between patients with and without the therapy (65% versus 56%, $P = 0.13$ by log-rank test) (Fig. 5). Furthermore, neoadjuvant chemotherapy did not influence the overall survival among all clinical stages. Similarly, adjuvant chemotherapy did not improve the prognosis because the 5-year overall survival rates for all patients with and without this therapy were 57% and 56%, respectively. When we investigated the influence of adjuvant chemotherapy on the 5-year overall survival in patients with pT2 or a lower stage without lymph node metastasis, there was no significant difference between patients with and without the therapy. No survival benefit was found for the therapy in patients with pT3 or pT4 without pathologically proven lymph node metastasis. However, the therapy improved the 5-year overall survival in patients with lymph node metastasis, with a significant difference between those with and without it ($P < 0.001$, by log-rank test) (Fig. 6).

DISCUSSION

In this study we evaluated the treatment outcomes of patients with invasive bladder cancer who underwent radical cystectomy with/without pelvic lymph node dissection in 21 hospitals from 1991 to 1995. The study enabled us to analyze the 5-year survival rates of a large volume of patients. The analysis showed that the 5-year overall survival rate for patients with T2N0M0, T3N0M0 and T4N0M0 tumors were 67%, 52% and 38%, respectively. These results are similar to/better than a previous report that the 5-year survival rates were 49% (95% CI: 39–59%) for patients with T2, 25% (95% CI: 10–50%) for those with T3 and 17% (95% CI: 5–45%) for those with T4,

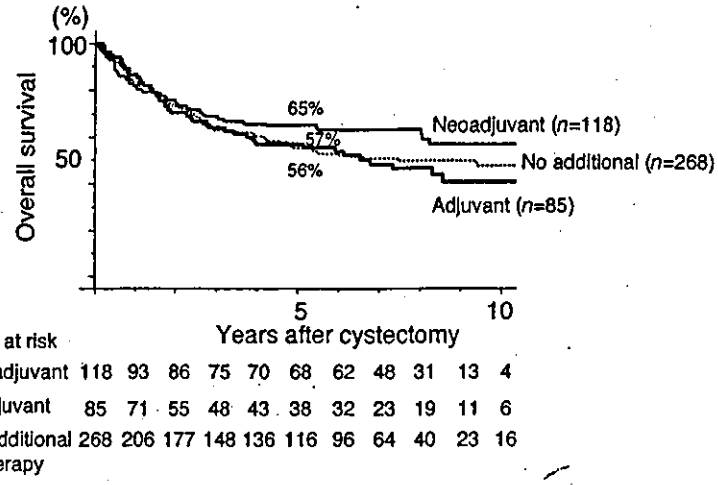


Figure 5. Overall survival rate according to additional therapy. Neoadjuvant versus no additional therapy, $P = 0.13$ (log-rank test); adjuvant versus no additional therapy, $P = 0.72$ (log-rank test).

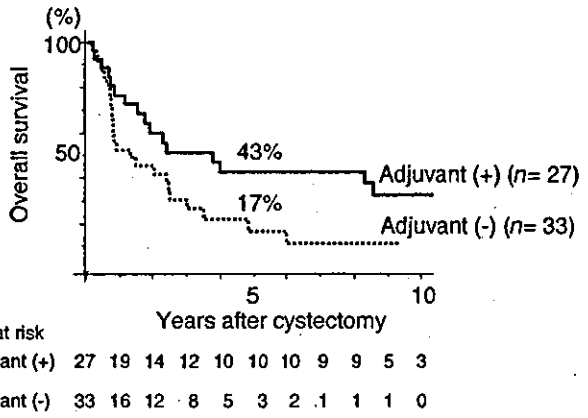


Figure 6. Overall survival rate according to adjuvant therapy in patients with lymph node metastasis. Adjuvant (+) versus adjuvant (–), $P = 0.03$ (log-rank test).

although this report was published 10 years ago (10). Similarly, the analysis according to pathological stage revealed results consistent with those in previous studies showing that the 5-year survival was 76–85% for pT1 or lower stage, 64–84% for pT2pN0, 25–56% for pT3pN0 and 19–44% for pT4pN0 (1,11,12). In Japan, the analysis of 351 patients who underwent radical cystectomy at a single institute showed a similar result (13).

In the present study pathologically proven lymph node metastasis was seen in 18% of patients with lymph node dissection. Some reports indicated that lymph node metastasis was present in 15–34% of patients who underwent radical cystectomy (10,14–16). The variation in the incidence of positive nodes may stem from the heterogeneous profiles of patients, extent of lymph dissection, and the number of lymph nodes removed. Indeed, Leissner et al. (14) reported a correlation between the number of lymph nodes removed (≥16 lymph nodes) and the percentage of patients with positive nodes, especially in locally advanced bladder cancer. Lymph node metastasis is reported to be an independent poor prognostic factor (14–16). Our study supported previous results since the present study also showed that patients with positive nodes had a worse prognosis. Recently, the number of positive lymph nodes, rather than the size, was reported to be associated with death from bladder cancer (15,16). Unfortunately we did not assess the number of lymph nodes in this study. Further study will be necessary to confirm these results. At present it remains controversial whether lymph node dissection has a therapeutic effect or is merely a staging tool. Some investigators advocate extensive bilateral lymphadenectomy as a potentially curative procedure (14,16).

Since the 5-year survival rate with radical cystectomy alone seems to reach a plateau, especially in patients with locally advanced bladder cancer, various trials of additional treatments before and/or after surgery have been carried out (3–5). Unfortunately, it remains undefined whether neoadjuvant or adjuvant chemotherapy with surgery improves the survival (17). However, in the SWOG study, patients with three cycles of neoadjuvant MVAC achieved survival benefit with the median survival of 77 months, as compared with 46 months among patients with surgery alone, although the difference was not significant when it was analyzed by a two-sided stratified log-rank test (6). Furthermore, more recent meta-analysis demonstrated that neoadjuvant cisplatin-based combination chemotherapy provided a survival advantage over a definitive local therapy (7). Our group started a prospective phase III study evaluating the survival benefit of two cycles of MVAC followed by surgery over surgery alone in patients with T2–4N0M0 bladder cancer with the support of the Japanese Clinical Oncology Group.

On the other hand, our retrospective study showed that patients with lymph node metastasis had a survival benefit from adjuvant chemotherapy, although only a small number of patients were included. Some investigators also reported the impact of adjuvant chemotherapy on survival of these patients in retrospective studies (15,16). Furthermore, prospective studies demonstrated a significant survival benefit (18–20). However, these studies were criticized due to their small

numbers of patients, early termination of trials and confusing methodology for analysis. Therefore, the role of adjuvant chemotherapy remains a matter of debate. To evaluate the impact of immediate adjuvant chemotherapy after cystectomy, the European Organization for Research and Treatment of Cancer has launched a large randomized trial that plans to enroll 1344 patients. In the near future its results will tell us whether immediate adjuvant chemotherapy is necessary in high-risk patients.

In summary, our retrospective, multi-institutional analysis showed that radical cystectomy provided an overall survival for patients with clinically invasive bladder cancer similar to that of previous reports. Thus, it is clear that surgery alone will not provide better survival than we have now. Therefore, additional therapy is mandatory to improve the treatment outcome. Further large-scale randomized studies will be needed to clarify the timing and type of additional therapy.

Acknowledgments

The urologists listed below significantly contributed to data collection of this study. Shin Suzuki (Hokkaido University Graduate School of Medicine), Norihiko Tsuchiya (Akita University School of Medicine), Kazutoshi Yamana (Niigata University Graduate School of Medicine and Dental Sciences), Yasuo Kitamura (Niigata Cancer Center Hospital), Shinya Kobayashi (Shinshu University School of Medicine), Toyofusa Tobe (Chiba University Graduate School of Medicine), Yasunobu Hashimoto (Tokyo Women's Medical University School of Medicine), Shigeru Watanabe (Toranomon Hospital), Kiminobu Arima (Mie University Faculty of Medicine), Osamu Kamihira (Nagoya University Gradate School of Medicine), Yutaka Ono (Osaka Medical Center for Cancer and Cardiovascular Diseases), Hiroyuki Nishiyama (Kyoto University Graduate School of Medicine), Kiyohide Fujimoto (Nara Medical University), Tadashi Hayashi (Japan Red Cross Wakayama Medical Center), Kyohei Kurose (Okayama University Graduate School of Medicine and Dentistry), Masashi Inui (Kagawa University Faculty of Medicine), Makoto Satoh (Tohoku University Graduate School of Medicine), Yoshihiro Wada (Kumamoto University School of Medicine), Yoshiharu Imazono (Kagoshima University School of Medicine). This work was supported in part by a Health and Labor Sciences Research Grant (Clinical Research for Evidenced Based Medicine) from the Ministry of Health, Labor and Welfare of Japan.

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Reprinted from
Jpn J Clin Oncol 2004;34(2)78–81

Dynamic Computed Tomography and Color Doppler Ultrasound of Renal Parenchymal Neoplasms: Correlations with Histopathological Findings

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Received September 22, 2003; accepted December 13, 2003

Background: We evaluated whether color Doppler ultrasound (US) had diagnostic accuracy equal to dynamic computed tomography (CT) and whether performing dynamic CT and Doppler US together would be more informative in preoperative diagnosis of renal solid tumors.
Methods: A total of 110 renal solid tumors smaller than 7 cm were evaluated with dynamic CT and Doppler US. We compared the enhancement and the color flow patterns with the histopathological subtypes.
Results: Eighty-seven (95.6%) of 91 clear cell carcinomas showed rich enhancement in the cortical nephrographic phase (CNP) and 82 (90.1%) of them had color flow in the Doppler US. Of the total of 110 tumors, nine (8.1%) did not show color flow in spite of rich enhancement in the CNP. Conversely, eight (7.2%) of the 110 tumors showed color flow in spite of poor enhancement, including two chromophobe cell carcinomas and two metastatic renal tumors.
Conclusions: The enhancement pattern in dynamic CT and the color flow pattern in Doppler US were different among the subtypes of RCC. Color Doppler US had diagnostic accuracy equal to dynamic CT in most patients with renal solid tumors. Although Doppler US may play a unique role in the diagnosis of some renal parenchymal solid tumors, it is sufficient to perform dynamic CT alone for diagnosis of clear cell carcinoma.

Key words: color Doppler ultrasonography – computed tomography – kidney – neoplasm – renal cell carcinoma

INTRODUCTION

In recent years, computed tomography (CT) and ultrasound (US) have dramatically improved the early detection of renal masses. Most renal cell carcinomas (RCCs) are characterized by abnormal vascular structures (1). Dynamic CT is an established method of imaging renal masses and evaluating their vascularity via pooling of contrast medium in the tumor (2). Clear cell carcinoma (conventional RCC) is described as an attenuated tumor in the arterial phase of dynamic CT (3). The enhancement pattern in dynamic CT has been reported to be different among the subtypes of renal cell carcinoma (4). To the best of our knowledge, however, there has been no report showing the patterns of color Doppler US among the subtypes of renal neoplasms. Moreover, some patients are allergic to the contrast medium used for dynamic CT and patients are also exposed to a large amount of X-rays in CT scanning. Hence there is a need for diagnosis of RCC by another method less invasive than CT. Doppler US allows for non-invasive assessment of vascular flow signals from neovascularity in tumors (5). Thus, we first hypothesized that color Doppler US may also show different patterns like dynamic CT findings. Second, we also hypothesized that we could obtain more accurate information about the histopathological subtypes of renal parenchymal neoplasms if both dynamic CT and color Doppler US were performed. In this study, we compared the histopathological distribution of the dynamic CT findings for renal solid tumors with the color Doppler US findings and evaluated whether dynamic CT is more informative in preoperative diagnosis of renal solid tumors.

PATIENTS AND METHODS

PATIENTS

Between August 1996 and May 2001, 110 patients with solid masses smaller than 7 cm in diameter and with pathological

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results confirmed by surgical removal of tumors were eligible for this study. The patients (75 men and 35 women) ranged in age from 22 to 85 years (median 62 years) and tumor size ranged from 1.0 to 7.0 cm (median 3.6 cm) in diameter. These patients were suspected to have RCC by US and/or CT at other hospitals and were introduced to us for further evaluation and treatment of those tumors. By initially performed B-mode US, angiomyolipomas (AMLs) were excluded.

Dynamic CT

Dynamic CT was performed using a Toshiba X-Vigor with 7 mm/s table feed for 7 mm slice helical scans. An unenhanced scan was carried out initially to obtain baseline attenuation values of lesions and to identify calcification. After bolus administration of 100–120 ml of contrast medium intravenously (injection rate 2.5–3.0 ml/s), two phases of renal enhancement were recognized. Initially, 30 s after the contrast medium injection, there was enhancement of the cortex, but not the medulla, so that cortical nephrographic differentiation was seen [cortical nephrographic phase (CNP)]. Five minutes after the injection, additional scanning was performed to obtain images of its excretion by the pelvic caliceal system (excretory phase). If the tumor density in the CNP was higher than that of the renal medulla, it was defined as rich enhancement. If it was lower than that of the renal medulla but higher than that in the pre-enhancement phase, it was defined as poor enhancement.

Color Doppler US

Color Doppler US examinations were performed with commercially available real-time scanners (Toshiba SSA380A) by the same senior radiologist (Y.M.). The radiologist had no information about the dynamic CT findings. Patients were examined in the supine and lateral decubitus positions, using transverse, intercostal and parasaggital scanning. The insonating frequency of the sector scanner was 4.7 mHz. The Toshiba unit incorporates a real-time scanner and range-gated pulse Doppler velocity meter. The wall filter was set as low as possible and the real-time B-mode was used to locate the tumors. The Doppler US scanning was performed under conditions of no color flow in the normal renal parenchyma. If color flow was detected in the tumor, it was defined as positive flow.

Classification

Histopathological findings were reviewed for the subtypes of neoplasms, according to the classifications of the Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC) (6). By the findings and estimation of detection of early enhancement patterns in dynamic CT and color flow in Doppler US, four distinct patterns could be identified: group 1, tumors with both rich enhancement and color flow; group 2, with rich enhancement and without color flow; group 3, with poor enhancement and with color flow; and group 4, with poor enhancement and without color flow.

Table 1. Histopathological findings and patterns of dynamic CT and Doppler US

	Group 1	Group 2	Group 3	Group 4	Total
Enhancement in CNP of CT	+	+	–	–	
Color flow in Doppler US	+	–	+	–	
Clear cell carcinoma	81	6	1	3	91
Papillary RCC	1		1	3	5
Granular cell carcinoma	1	2	1		4
Chromophobe cell carcinoma			2		2
Spindle cell carcinoma	1		1		2
Collecting-duct carcinoma		1			1
Metastatic renal tumor			2		2
Benign renal tumor	3				3
Total	87	9	8	6	110

CNP: cortical nephrographic phase.

RESULTS

Histopathological Distribution of All 110 Tumors

Histopathological examination revealed that, of the 110 neoplasms, 91 were clear cell carcinomas, five were papillary RCCs, four were granular cell carcinomas, three were benign renal tumors, two were chromophobe cell carcinomas, two were spindle cell carcinomas, two were metastatic renal tumors and one was a collecting-duct carcinoma.

One of the metastatic tumors was malignant melanoma. There were no other metastatic sites in the patient. The other was thyroid papillary cancer. Although the patients also had lung, retroperitoneal and mediastinal lymph node metastases, primary renal neoplasm could not be denied because only the renal tumor had grown in a short time.

The three benign tumors were composed of an oncocytoma, a leiomyoma and an AML.

Patterns of Dynamic CT and Color Doppler US (Table 1)

Group 1 (n = 87)

Eighty-one (93.1%) of the 87 tumors were clear cell carcinomas. The remainder consisted of one granular cell carcinoma, one papillary RCC, one spindle cell carcinoma and three benign tumors (an AML, an oncocytoma and a leiomyoma). All the benign tumors were diagnosed as renal cell carcinoma before the surgical treatment.

Group 2 (n = 9)

Six (66.7%) of the nine tumors were clear cell carcinomas. The others were two granular cell carcinomas and one collecting-duct carcinoma.

GROUP 3 (n = 8)

The group three tumors consisted of two chromophobe cell carcinomas, two metastatic tumors, one clear cell carcinoma, one granular cell carcinoma, one papillary RCC and one spindle cell carcinoma. The histological diagnoses of the metastases were papillary thyroid cancer and malignant melanoma.

GROUP 4 (n = 6)

Three papillary RCCs and three clear cell carcinomas were identified. Two of the clear cell carcinomas had atypical structures; they were only tubular and solid with a small tubular part, respectively. The remaining one had severe arteriosclerosis of the renal artery.

DISCUSSION

Recent advances in US, CT and magnetic resonance imaging (MRI) techniques have enabled us to detect incidentally renal cell carcinomas (7,8). In our institute, most renal parenchymal neoplasms were first suspected by physicians to be RCCs in the process of examinations for non-urological diseases. After the diagnosis as a renal parenchymal solid tumor other than AML, we performed dynamic CT and confirmed the diagnosis as RCC before the surgical treatment because dynamic CT has been the most readily available method for diagnosis of RCC, including subtypes (3,4). However, it is essential for a diagnosis of RCC to use contrast medium in dynamic CT and patients are irradiated with a large amount of X-rays. Moreover, we sometimes cannot confirm the diagnosis of a renal malignant tumor by dynamic CT even if AML is denied by B-mode US. Therefore, we studied the efficacy of color Doppler US for the diagnosis of renal parenchymal neoplasms.

Doppler US is at least as accurate as CT in staging of RCC (9) and may improve the accuracy of US determination of malignancy (10). However, to the best of our knowledge, there has been no report on correlations between the color flow patterns and the subtypes of RCC. The relationship between dynamic CT and color Doppler US findings also has not been reported. We previously reported that clear cell carcinoma with alveolar architecture showed a highly attenuated area in the CNP of dynamic CT (3). Jinzaki et al. (4) also reported that clear cell carcinoma showed a peak attenuation value in the CNP of >100 HU, whereas for other subtypes the values were <100 HU. The attenuation patterns of the tumors in this study were mostly consistent with those reported previously. Since the color flow positive rate of our tumors was similar to the dynamic CT positive rate, it was suggested that color Doppler US was as readily applicable as dynamic CT for diagnosis of renal parenchymal neoplasms. However, there were some tumors without color flow in Doppler US in spite of rich enhancement in dynamic CT. Conversely, there were also some tumors with color flow in spite of poor enhancement in CT.

In our series, color Doppler US showed color flow in chromophobe cell carcinomas despite the fact that dynamic CT showed poor enhancement of these tumors. Although it is too early to discuss our small number of chromophobe cell carcinomas, it has been reported that chromophobe cell carcinoma has a peak attenuation value in the CNP in dynamic CT of <100 HU (4). It may be better to perform additional color Doppler US if dynamic CT does not demonstrate a highly attenuated tumor.

Doppler US also showed color flow in metastatic renal tumors. However, the number of our patients was too small to analyze the characteristics of such tumors. The findings of dynamic CT and color Doppler US might be different for each primary tumor.

In this study, three benign tumors were diagnosed as RCC both by dynamic CT and color Doppler US. Jinzaki et al. (4) reported that it was too difficult to differentiate RCC and other benign tumors (oncocytoma and metanephric adenoma) by dynamic CT. We suggest that there is no difference between the false-positive rates of dynamic CT and of Doppler US in diagnosis of renal parenchymal tumors and that another diagnostic method is necessary to differentiate between them. In contrast, there were six tumors (three papillary RCCs and three clear cell carcinomas) diagnosed as non-RCC by both CT and Doppler US. Most papillary RCCs show hypovascularity (11) and lower enhancement in the cortical nephrographic phase of dynamic CT than clear cell carcinoma (4). Choyke et al. (12) reported that the tumors of patients with hereditary papillary renal cancer syndrome posed some diagnostic difficulties because they could be missed by US, were small and enhanced poorly on CT. Moreover, even if the histological cell type is clear cell carcinoma, the hypervascularity on the CNP of dynamic CT is not shown if the architecture of the tumor is not the alveolar type (3). Therefore, new diagnostic methods are needed for the diagnosis of those tumors. It may be possible to clarify the discrepancies between the Doppler US and the dynamic CT findings by using some new diagnosis modalities, e.g. contrast-enhanced Doppler US. However, a prospective study with a large number of patients is needed to clarify the efficacy.

The reproducibility of color Doppler US might be doubtful, although a senior radiologist performed color Doppler US for all the patients in our series. Dynamic CT is superior to Doppler US in this respect. However, color Doppler US is performed safely for patients who are allergic to contrast medium or who are pregnant. Although it is sufficient to perform dynamic CT alone for the diagnosis of renal solid tumors in most patients, color Doppler US can be used instead of dynamic CT in patients whose tumor is poorly attenuated or who have problems with using contrast medium, exposure to radiation, etc.

In conclusion, we can diagnose renal solid tumors by dynamic CT alone in most patients, although the enhancement pattern in dynamic CT and the color flow pattern in Doppler US are different among the subtypes of RCC. Doppler US may play a unique role in the diagnosis of some renal parenchymal solid tumors. However, more data on chromophobe cell carcinoma, metastatic renal cancer, etc., are needed.

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