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Demonstration of renal arterial anatomy and tumour neovascularity for vascular mapping of renal cell carcinoma: the value of CO_2 angiography

C SANDHU, MRCP, FRCR, A M BELLI, FRCR and U PATEL, MRCP, FRCR

Department of Radiology, St George's Hospital, Blackshaw Road, London SW17 0QT, UK

Abstract. The aim of this study was to compare the efficacy of CO_2 angiography with that of iodinated contrast angiography for vascular mapping prior to partial nephrectomy for presumed renal cell carcinoma. 13 consecutive patients were studied and all patients underwent selective renal angiography using both CO_2 and iodinated contrast medium. Digitally subtracted images were acquired and compared. Seven male and six female patients, with a median age of 58 years (range 46–74 years), were examined. On comparing images the main renal artery was visualized in all cases with both contrast agents. The segmental vessels were seen in 7 of 13 CO_2 studies and 12 of 13 iodinated contrast studies. CO_2 was also inferior in the depiction of tumour circulation, showing it in 4 of 13 cases compared with 9 of 13 cases using iodinated contrast. It therefore appears that CO_2 angiography offers no diagnostic advantage and is also inferior to iodinated contrast angiography in the pre-operative vascular mapping of renal tumours.

Introduction

Over recent years partial nephrectomy, or nephron sparing surgery, has become an accepted technique in the management of renal cell carcinomas (RCCs) [1, 2]. These include neoplasms occurring in patients with diminished renal function, a solitary kidney or tumours in both kidneys. Increasingly, partial nephrectomy is also the preferred approach for small RCC in patients with otherwise normal kidneys [3]. Good vascular control is important during this operation and is achieved by cross-clamping the main renal artery, followed by division of the tumour supplying divisional or segmental branches [4].

Identification of these tumour-supplying vessels can be performed intraoperatively but many surgeons prefer precise pre-operative vascular mapping and, in particular, prior knowledge of the number and origin of the divisional and segmental arteries. Standard iodinated contrast angiography has an established role [5, 6]. However, this method is potentially nephrotoxic and may be contraindicated in patients with impaired renal function. Furthermore, a significant number of small tumours may not demonstrate angiographically visible neovascularity [7].

CO_2 enhanced angiography may overcome these shortcomings, as it has no reported nephrotoxicity [8]. CO_2 enhanced angiography possesses a number of favourable physical characteristics, such as a lack of dilution and low viscosity, which may allow clearer demonstration of tumour circulation when compared with conventional angiography.

This study was designed to prospectively evaluate the advantages of CO_2 arteriography in vascular mapping prior to partial nephrectomy.

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Subjects and methods

13 consecutive patients with a presumptive diagnosis of renal cell carcinoma, and referred for angiographic assessment prior to intended partial nephrectomy, were studied. In all cases a presumptive diagnosis of RCC was made on contrast enhanced CT (IGE HiSpeed CTI; General Electric Medical Systems, Milwaukee, WI) or MRI (IGE 1.5T; General Electric Medical Systems, Milwaukee, WI).

Following informed consent all patients underwent iodinated and CO_2 angiography, using a standard protocol. Appropriate approval had been granted by the local research ethics committee. A transfemoral approach and selective femorovisceral catheters (Cobra 5 F; Terumo, Tokyo, Japan) were used to catheterize the renal artery. CO_2 was delivered using an automated injection system (CO2JECT; Angiodynamics, Glens Falls, NY). The volume of CO_2 injected was 30–50 ml at flow rates of 10–15 ml s^{-1}. Iodinated contrast angiography was performed using 25–30 ml iopamidol (Niopam; Bracco, Milan, Italy) delivered by automated injector at 5 ml s^{-1}. With both contrast agents, multiple projection digitally subtracted images were acquired on an Advantx LCA angiography system (General Medical Systems, Milwaukee, WI) following intra-arterial administration of 150 μg glyceryltrinitrate (Nitronal; Lipha Pharmaceuticals Ltd, West Drayton, England), to relieve catheter-induced arterial spasm, and 20 mg hyoscine-N-butyl bromide (Buscopan; Boehringer Ingelheim, Bracknell, England), to minimize bowel peristalsis. On average the ratio of CO_2 acquisitions to iodinated contrast acquisitions was 2:1. Images were acquired during suspended respiration, with side of interest elevated to 90° for CO_2 injections, at a rate of three per second for the first 6 s and every second thereafter to a maximum of 30 s. Images were acquired in the same projection for each contrast agent. If images were considered inadequate, repeat acquisitions were performed after adjusting contrast volumes and flow rates and/or mAs and kv. A 1024 × 1024 imaging matrix was used and images were

post-processed and re-masked. Minimum opacification software was not available for post processing. Selected images were stored on hard copy and a complete videotape record of each examination was also made.

All studies were reviewed immediately after the study by the operator, and later by an independent reviewer. The following aspects were specifically scrutinized for both CO_2 and iodinated contrast studies:

- Was the main renal artery clearly seen?
- Were the small intrarenal arterial branches (arcuate and interlobular or corticomedullary branches) well seen?
- Was the tumour circulation/neovascularity seen?

A subjective two point scale was used to grade the diagnostic value of each acquisition. If a given artery/branch was clearly visualized in its entirety as contrast filled without any breaks, the study was considered diagnostic and scored 1. Arteries with beading or break-up of contrast or only partially visualized were judged non-diagnostic for the purposes of confident vascular mapping and scored 0. For tumour vascularity, any of the following were taken as signs of its presence: irregular, branching vessels; arteriovenous shunts; or lakes (score 1). Indirect signs of tumour or mass effect, such as the displacement or splaying of vessels, were considered unreliable signs for accurate vascular mapping and were not specifically categorized.

Results

Seven male and six female patients, with a median age of 58 years (range 46–74 years), were examined. No complications related to angiography were observed. Details of tumour size and histology are summarized in Table 1. Seven patients had RCC confirmed on histology. One patient was diagnosed with an angiomyolipoma. This had minimal fat on histology, and review of the CT dataset revealed only isolated clusters of fat densities on pixel mapping, which had not been apparent at the initial reading of the CT when region of interest density measures had been used alone. The patient with foreign body reaction had previously undergone partial nephrectomy for a proven RCC in another hospital and Surgicel (Johnson and Johnson Medical Inc., Arlington, TX) had been used intraoperatively to control bleeding. He had re-presented with a new small, solid mass in the same kidney, which showed minimal enhancement (CT density increment of 13 units post contrast) and this was interpreted as a new RCC. The details of this case have already been published [9]. Of the four remaining patients, no histology was available as these patients either refused surgery or were unsuitable for surgery and underwent chemotherapy or embolisation (n=2).

Table 2. Vessel visualization according to contrast agent used

Branch vessel	No. of cases	
	Iopamidol	CO_2
Main renal artery	13 (100%)	13 (100%)
Divisional	13 (100%)	13 (100%)
Segmental	12 (92%)	7 (54%)
Corticomedullary	13 (100%)	0
Tumour circulation	9 (69%)	4 (31%)

On comparing the angiographic studies there was agreement between the two observers. The main renal artery was well visualized in all cases with both contrast agents (Table 2). No significant variant anatomy was demonstrated. The intrarenal arterial architecture was better visualized with the iodinated contrast injections, particularly at the segmental level and beyond (Figure 1, 2). CO_2 was also inferior in the depiction of tumour circulation, showing it clearly in 4 of 13 cases compared with 9 of 13 cases for iodinated contrast injections.

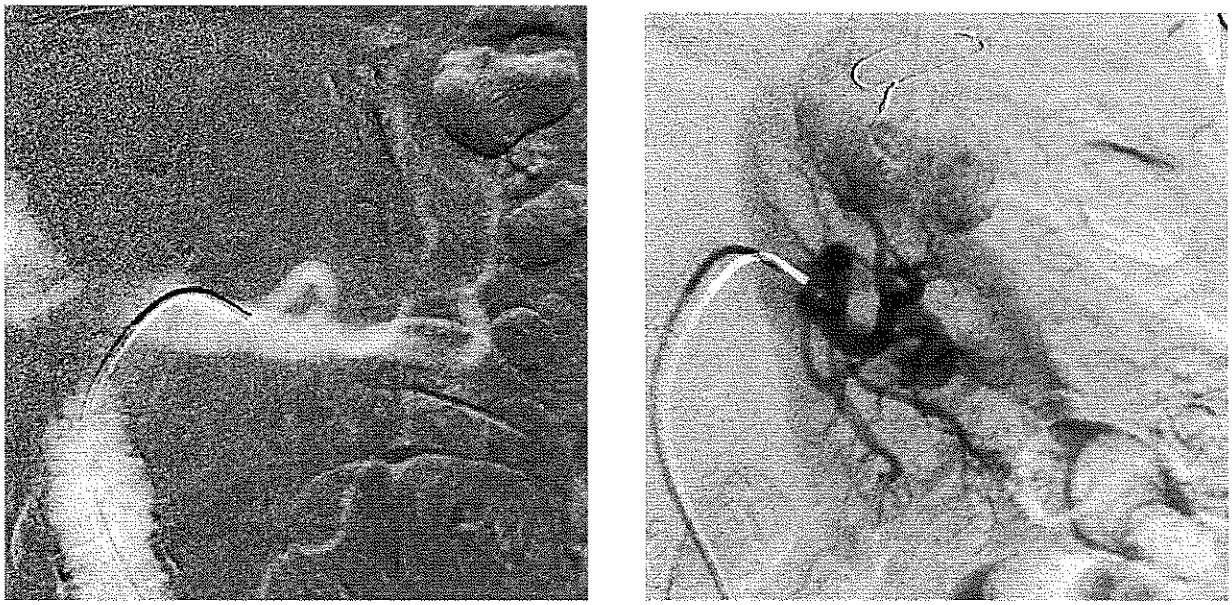
Discussion

With the advent of multiplanar imaging techniques such as helical CT and MRI, the role of angiography in patients with RCC has reduced. Angiography also has a negligible role in the evaluation of the indeterminate renal mass, as state-of-the-art CT or MRI will accurately determine the nature of such lesions without recourse to angiography. However, it continues to have a small role in the pre-operative planning of known or suspected renal cancer when precise arterial mapping is required. These include

Table 1. Tumour size and histology in patients studied

Patient	Tumour size (cm)	Histology	Demonstration of tumour circulation	
			CO_2	Iopamidol
1	9.0	RCC (papillary)	0	0
2	3.0	n/a	0	1
3	1.3	RCC (papillary)	0	0
4	3.0	RCC (clear cell)	0	1
5	4.0	RCC (clear cell)	1	1
6	13.0	n/a	1	1
7	4.0	RCC (clear cell)	1	1
8	3.0	Foreign body reaction	0	0
9	2.5	RCC	0	0
10	1.5	RCC	0	1
11	1.5	Angiomyolipoma	0	1
12	20	n/a (embolised)	1	1
13	4.0	n/a (embolised)	0	1

RCC, renal cell carcinoma; n/a, not available; 0, absent; 1, present.



(a) (b)

Figure 1. (a) 74-year-old man with 4 cm left renal mass. Digitally subtracted selective left renal angiogram (CO_2) demonstrates the divisional and segmental arteries. Fragmentation of the CO_2 bolus prevents visualization of the corticomedullary and tumoral vessels. (b) The mass and feeding vessels are clearly demonstrated using iodinated contrast medium.

some patients considered suitable for nephron sparing surgery, especially those with a tumour arising in a solitary kidney, a kidney with variant anatomy, *e.g.* horseshoe or pelvic kidney, or those with tumour in both kidneys [5].

For accurate mapping, the intrarenal architecture, tumour circulation and nephrograms should all be clearly visualized so that all tumour supplying branches, be they at the divisional or segmental level, can be individually identified and isolated. Precisely controlled angiography is therefore required, such that the deepest portions of the arterial tree are well filled with contrast. Selective and, if necessary, super-selective catheterization is essential, as well as the use of high quality digital subtraction techniques. In spite of this, in some patients iodinated contrast arteriography is inadequate, chiefly because of failure to demonstrate tumour circulation. In this study tumour circulation was seen in only 9 of 13 patients. This may be owing to the relative hypovascularity of some RCCs, such as complex malignant cysts and small renal cancers [7].

In order to improve the diagnostic information from angiography, particularly the visualization of tumour circulation, this study focused on the potential benefits of CO_2 angiography. Previous articles, such as that by Hawkins and Caridi [8], have commented on the theoretical benefits of CO_2 in the demonstration of tumour neovascularity, as these are vessels of low peripheral resistance because they lack a complete muscle layer in the neoarteries and have numerous arteriovenous shunts. CO_2 has a much lower viscosity than iodinated contrast, approximately 1:400 compared with standard non-ionic iodinated contrast media, and displaces rather than mixes with blood. These two properties should ensure maximal concentrations of the agent within the low resistance tumoural circulation. However, these proposed advantages have not been proven and no study specifically of the value of CO_2 in demonstrating deep intrarenal arterial anatomy has been undertaken. In our series, CO_2 enhanced angiography was inferior to iodinated contrast angiography, both with respect to demonstration of renal vascular anatomy as well as the neovascularity of the tumour mass.

The reasons for these findings are unclear and small sample size may be a factor. The technical factors used were optimized for diagnostic CO_2 angiography [7]. The patient was correctly positioned, vessels were selectively catheterized and adequate boluses of CO_2 were delivered using an automated system, to obviate the problems of explosive delivery [7]. However, despite these measures, the CO_2 enhanced images lacked both the contrast and spatial resolution of those acquired using standard iodinated contrast. One possible explanation is that even though the studies were carried out with side of interest elevated, some parts of the renal arterial tree remain relatively dependent and do not fill with gas, even with the use of large gas boluses. The poor visualization of intrarenal branches has been previously commented upon. Schreier et al [10] found that they visualized 85%, 47% and 20% of divisional, segmental and corticomedullary branches, respectively. But our feeling is that early fragmentation of the CO_2 bolus appears to be the major, and seemingly insurmountable, limitation to using CO_2 for the demonstration of detailed tissue and tumour vascularity. The factors that lead to bolus fragmentation have not been specifically studied, but subjectively it is more noticeable around arterial junctions, and physical forces such as turbulence may have a role. Future advances in imaging software may overcome this limitation but currently we would not recommend the routine use of CO_2 angiography in the evaluation of renal tumours and tumour vascularity.

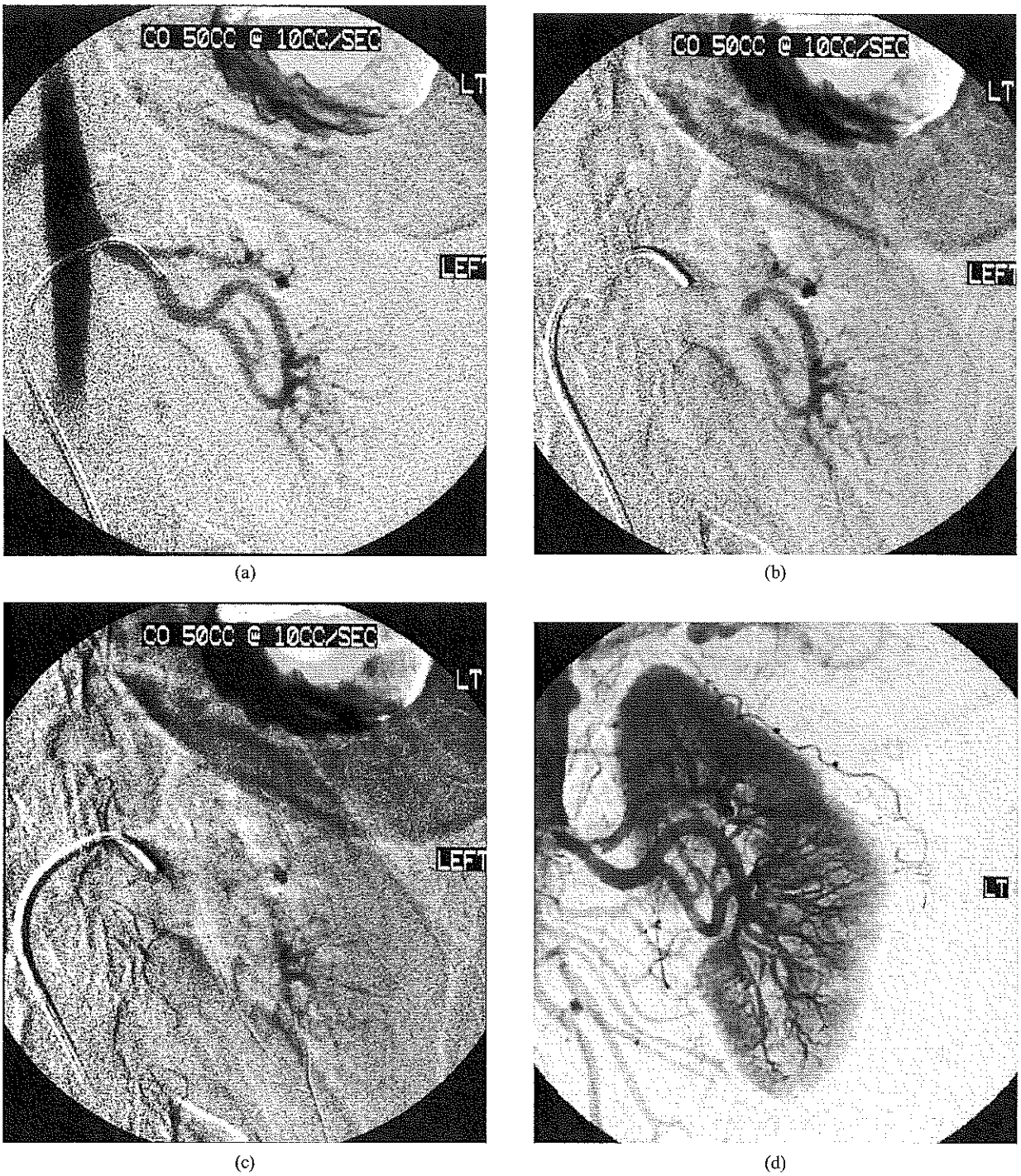


Figure 2. (a–c) 56-year-old lady with a 1.3 cm left renal mass. Digitally subtracted selective left renal angiogram (CO_2) demonstrates poor opacification of the intrarenal vessels through all phases of the acquisition. No tumour blush is seen. (d) The corresponding study using iodinated contrast demonstrates all intrarenal vascular divisions as well as capsular vessels, which may be contributing to tumour supply. However, the tumour is not easily visualized.

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