Correspondence

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Reply to R Loffroy's letter to the Editor re: M May et al. Pre-operative renal arterial embolisation does not provide survival benefit in patients with radical nephrectomy for renal cell carcinoma. Br J Radiol 2009;82:724–31.

The Editor — Sir,

We would like to comment on the letter to the Editor by Loffroy, Rao, Ota and Geschwind [1]. We appreciate the insightful comments of Loffroy and colleagues regarding pre-operative renal arterial embolisation (PRAE) in patients with renal cell carcinoma (RCC) [2]. They refer to some important points relating to PRAE, to which we would like to respond.

Issue 1: Different median follow-up in the two groups

In their letter to the editor, Loffroy and colleagues suggest that our results could have been biased by a different mean follow-up of patients with and without PRAE (99.7 *vs* 62.3 months, respectively). We agree with this comment: comparing a historical group of patients (PRAE between 1992 and 1997) with current patients (nephrectomy alone between 1992 and 2006) resulted in a varying mean follow-up time. However, in the last part of our discussion we referred to this problem with the method [2]. By contrast, owing to the overall long follow-up time in both groups, the 5-year survival rates are robust and, therefore, comparable between the two groups of patients. Regarding 5-year survival rates, we did not find any significant differences for cancer-specific survival (79% *vs* 83%) or for overall survival (73% *vs* 75%) between patients with and without PRAE.

On no account should our study be perceived as a prospective controlled study; patients were matched with respect to oncological and baseline characteristics by using a propensity score that included nine relevant variables (age, gender, clinical tumour size, grading, pN stage, cM stage, pT stage, histology and microvascular invasion).

Issue 2: Advances in medical management, surgical approaches and interventional techniques during follow-up

We totally agree with the objection that advances in medical management have occurred over the study period; however, PRAE was still performed in a standardised way (*quod vide* methods section [2]). Advances in surgical approaches have been marginal; however, in the last part of the discussion we pointed out

that there had been an increasing use of nephron-sparing surgery during the period of investigation.

Issue 3: PRAE as a technique that facilitates nephrectomy

We agree with this comment. However, references relating to this point were reported and discussed in our paper [3–5]. It is reasonable to use pre-operative embolisation of the tumour-harboured kidney to decrease/avoid extensive blood loss during surgery and/or to facilitate surgery with huge renal tumours when the renal vessels are difficult to reach [3–5].

Issue 4: No specification of operating time

On the basis of our prospective database, the operating times of all performed nephrectomies have been analysed and compared for patients with ($n=227$) and without PRAE ($n=607$) (see Table 5 in May et al [2]). There was no significant difference between the mean operating time in both groups of patients (108 *vs* 102 min, respectively; $p=0.68$).

Issue 5: Clarification of blood transfusion requirements

It remains speculative as to why our results in respect of the blood transfusion requirements are not in concordance with other studies describing a reduction of the post-operative transfusion rate in patients with PRAE [3–5]. However, in the present study we compared a historical group of patients (PRAE between 1992 and 1997) with current patients (nephrectomy alone between 1992 and 2006), dealing with indications for administering blood transfusions in both groups. Recently, there have been many changes in transfusion practices and the indications for post-operative blood transfusions are very restrictive [6].

Issue 6: Clarification of the rate of post-embolisation syndrome and description of the protocol used for adjuvant pain medication

We compliment Loffroy and colleagues on their results and low rate of post-embolisation syndrome among their patients. In our patients with PRAE ($n=227$), symptoms of post-embolisation syndrome (including lumbar pain, fever, nausea, hypertension and macroscopic haematuria) have been prospectively recorded. In 202 patients (89%; see Table 5 in May et al [2]), symptoms have been reported with the vast majority being mild and self-limiting. These results are in accordance with other studies [7, 8].

As outlined in our article, in most patients (71%) embolisation was performed one to three days (median 1)

before surgery (not two to three days as pointed out by Loffroy et al). In our department, pain control after PRAE is standardised with oral/intravenous medication of non-steroidal anti-inflammatory agents and level 1/2 analgesics.

Issue 7: Controlled trials should be undertaken to compare the treatment of selected locally advanced RCC with or without PRAE

Despite the comments of our colleagues, we conclude that PRAE does not improve the survival of patients with renal cell carcinoma after surgery. Our current knowledge regarding possible benefits of PRAE is based on retrospective studies with only small cohorts of patients with heterogeneous characteristics. Nevertheless, we would like to quote the last sentence of our article [2]: "Further research, in particular prospective randomised clinical trials, is necessary to provide evidence for the pros and cons of this procedure reliably."

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New tools for allergy diagnosis and clinical advice after immediate reactions to ICM

The Editor — Sir,

Immediate adverse reactions to iodinated contrast media (ICM) are common in clinical practice, being classified as toxic (owing to osmolality, viscosity or ionising ability), non-immune hypersensitive (non-specific histamine release) or allergic (Type I or Type IV hypersensitivity) [1]. Traditionally, it has been considered that most immediate ICM reactions are caused by non-immune mechanisms (mainly non-specific histamine release); thus, preventive drug treatment and no further studies are advised. Nevertheless, at least in severe reactions, an allergy work-up could prove useful for the radiologist [2].

A 59-year-old man, an ex-smoker with thrombocytopenia who had never been exposed to ICM, suffered an ischaemic heart attack requiring coronary angiography. At the time of the procedure, he was on acetylsalicylic acid, clopidogrel, atorvastatin, atenolol, enalapril and nitrates. Fifteen minutes after the start of intravenous iodixanol (Visipaque® 320 I mL⁻¹; GE Healthcare Biosciences, Little Chalfont, UK) he complained of feeling hot, chills, faintness, dizziness and generalised rash; angioedema of trunk and limbs and hypotension developed. The procedure was then stopped and the patient fully recovered after volume reposition and administration of antihistamines and corticosteroids. A new coronary angiogram was scheduled 4 days later after a 24 h preventive antihistamine plus corticosteroid treatment, but the reaction happened again. An allergy work-up was therefore decided upon.

Skin-prick tests with all available non-ionic ICM (iobitridol, iodixanol, iohexol, iomeprol, iopamidol, iopromide, ioversol and ioxaglate) at full-strength concentration proved negative. Sequential intradermoreactions with 1:100 and 1:10 dilutions, at a 20 min reading, were strongly positive only for iodixanol 1:100 (*i.e.* 1:10 not performed). With the aim of seeking the theoretically best alternative, and according to Dewachter et al [4], ICM intradermoreactions with full-strength concentration were performed; these tests proved positive for iobitridol, iohexol, iopromide and ioversol. A basophil activation test (BAT) was strongly positive for iodixanol, iohexol and ioversol. As a result, iomeprol and ioxaglate, both with all negative allergy tests, were recommended for future administrations.

In the span of only 1 year, new facts and techniques have challenged our traditional concept of immediate adverse reactions to ICM. Brockow et al [2], in a multicentre European study, performed skin tests at concentrations up to 1:10 in 122 patients with a clinical history of immediate ICM reactions. These tests obtained a sensitivity of 26% (which reached 50% if the tests were performed between 2 and 6 months after the reaction) and a specificity of 96%. Moreover, they observed that almost half the patients (49%) and 43% of those with positive skin tests had never been exposed to ICM. Recently, Dewachter et al [4] performed ICM intradermoreactions at full-strength concentration (1:1) in 38 patients with immediate ICM reaction and obtained even higher sensitivity (73%). The argument that these positive intradermoreactions could correspond to irritating responses was counterbalanced by the fact that