SHORT REPORT

Assessment of the Cardiff nephrectomy cut-up protocol with total blocking of the renal sinus: effect on tumour staging and practical issues

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Aim: To evaluate the effects on detection of vascular invasion and workload of a new standard dissection protocol for examining nephrectomy specimens for renal cell carcinoma.

Methods: Using 192 consecutive renal cell carcinoma nephrectomy specimens, the incidence of vascular invasion and number of tissue blocks per tumour were compared before and after introduction of the new protocol.

Results: The Cardiff protocol increased the percentage of tumours staged as T3b (renal sinus or hilar vein invasion) from 37.7% to 55.7% cases ($p < 0.001$), with an increase from 9.1% to 21.7% of those staged as T3b due to renal sinus vein invasion alone ($p < 0.01$). A small, but significant, permanent increase in workload was observed from an average of 11.7 to 13.4 blocks per case ($p < 0.001$).

Conclusions: This protocol is suitable for use in routine practice to evaluate pathological prognostic determinants important for clinical management, while causing only a small increase in workload.

About two thirds of renal cell carcinomas (RCCs) are localised at presentation and these patients will usually undergo nephrectomy. Despite apparent complete tumour excision, metastasis will occur in up to 40% of patients, who subsequently die from their tumour.¹ Predicting those patients who will relapse is notoriously difficult and relies on pathological assessment of the surgically resected specimen.¹ Tumour size, stage and grade, the presence of vascular invasion and age of the patient are important prognostic features.^{1–3} Recent evidence suggests that a poor prognosis, with a higher risk of metastasis, is associated with renal sinus vein invasion (RSVI).⁴ The renal sinus is the fibro-fatty tissue housing the pelvi-calyceal and vascular structures passing between the parenchyma and hilum.⁵

The Royal College of Pathologists (UK and Ireland) minimum dataset (RCPATH minimum dataset) does not include a method of dissection for nephrectomy specimens for RCC. However, a dissection guide, describing the Cardiff protocol (used in this study), has recently been published.⁵ The new “Cardiff” dissection protocol advocates detailed examination and complete blocking of much or all of the renal sinus interface (materials and methods).⁵ An RCC may be staged as T3b due to either hilar or segmental venous invasion, provided there is some smooth muscle in the vessel wall.⁶ Segmental venous invasion refers to hilar vein tributaries in the renal sinus. The tumour–node–metastases staging system is not clear about whether an affected renal sinus vein should be visible macroscopically or just microscopically.⁶ The current RCPATH minimum dataset encourages

the recording of hilar venous invasion, but does not require comment on invasion of smaller vascular channels.

MATERIALS AND METHODS

In total, 500 nephrectomy specimens were received in the Histopathology Department of the John Radcliffe Hospital, Oxford, UK, during a 6-year period. Of these, 61.6% were excluded from the study because they were removed for non-neoplastic conditions, were benign tumours, were tumours of types other than RCC, or were partial or fragmented specimens. Of the remaining 192 nephrectomy specimens for RCC, 77 were dissected (1999–2001) before the switch to the Cardiff protocol⁵ and 115 (2001–2004) afterwards (table 1). All specimens were assessed or dissected by one of two renal pathologists or their closely supervised trainees, using similar block selection criteria. As in the Cardiff study, 10 blocks were taken initially, with subsequent additional blocks if vascular invasion was not identified, in an attempt to limit overall block numbers without compromising sensitivity.⁵

For each nephrectomy specimen, the following parameters were assessed: protocol used, total number of blocks, stage and presence of vascular invasion, divided into macroscopically visible hilar vein invasion (blocking renal sinus unnecessary) or sinus vein involvement only (identified macroscopically or microscopically). A renal sinus vein was defined as a venous channel in the renal sinus with at least some smooth muscle in its wall.⁶

Statistical analysis was carried out using Sigma Stat V.10, SPSS.

RESULTS

The protocol was easy to follow and teach. The mean number of blocks taken per case increased by 14.9%, from 11.7 to 13.4

Table 1 Number of nephrectomy specimens received at the John Radcliffe Hospital

Year	Total no of nephrectomy specimens	No meeting criteria for study	No (%) excluded
1999	67	27	40 (60)
2000	75	36	39 (52)
2001	69	35	34 (49)
2002	103	44	59 (57)
2003	84	23	61 (73)
2004	102	27	75 (74)

Abbreviations: RCC, renal cell carcinoma; RSVI, renal sinus vein invasion

Table 2 T stages of tumours included in the study

Parameter	Old protocol	New protocol	% change
Average no of blocks/case	11.7	13.4	+14.9 (p<0.001)
Stage T1a	16/77 (20.8%)	3/115 (2.6%)	-87.5
Stage T1b	9/77 (11.7%)	13/115 (11.3%)	-3.4
Stage T2	9/77 (11.7%)	16/115 (13.9%)	+18.8
Stage T3a	14/77 (18.2%)	10/115 (8.7%)	-52.2
Stage <T3b	48/77 (62.3%)	42/115 (36.5%)	-41.4 (p<0.001)
Stage T3b (total)	29/77 (37.7%)	64/115 (55.7%)	+47.7 (p<0.001)
Stage T3b (renal sinus vein invasion only)	7/77 (9.1%)	25/115 (21.7%)	+139.2 (p<0.01)
Stage T3b (renal vein invasion)	22/77 (28.6%)	39/115 (33.9%)	+18.7 (p>0.30)
Stage T3c	0/77 (0%)	5/115 (4.4%)	Increased
Stage 4	0/77 (0%)	4/115 (3.5%)	Increased

(p<0.001; table 2), and the median from 11 (range 6–26) to 13 (range 6–21).

The percentage of cases staged as T1, T2 or T3a (ie, no renal sinus vein or hilar vein invasion) decreased by 41.4% (from 62.3% to 36.5% (p<0.001); table 2), with major decreases in T1a (-87.5%) and T3a (-52.2%). Dissection with the Cardiff protocol was associated with a 47.7% increase in the number of cases staged as T3b (from 29/77 (37.7%) to 64/115 (55.7%); p<0.001), with a 139.2% increase in the number of cases staged as T3b due to RSVI alone (from 7/77 (9.1%) to 25/115 (21.7%); p<0.01).

The only difficulty encountered with the Cardiff protocol was deciding whether histological venous invasion was present. On a small number of occasions this required cutting of several levels on blocks with suspicious areas. Carcinoma within veins is generally continuous with the main tumour. The earliest stage is destruction of the muscular wall of the vein with the tumour covered only by endothelium (fig 1A). This is followed by intraluminal expansion of the tumour (fig 1B), then intraluminal extension away from the main tumour (fig 1C). RSVI was defined as those cases in which at least stage B could be shown histologically.

DISCUSSION

Our study confirms the findings from the Cardiff protocol⁵ and shows a 47.7% increase in the percentage of tumours staged as T3b (invasion of renal sinus/hilar veins), most of this increase resulting from cases with RSVI in the absence of renal hilar vein invasion. We advocate use of "renal sinus vein invasion", rather than "microvascular invasion", as, with experience, most of the cases can be identified by careful macroscopic examination. From our referral practice, it is apparent that many laboratories in the UK have not yet adopted the Cardiff dissection protocol and do not record RSVI. Although there is a small, but marked, permanent increase in workload, from an average of 11.7 to 13.4 blocks per case, we would advocate this method for the dissection of nephrectomy specimens for RCC.

Two problems were identified by this study. The first is the lack of clarity in the tumour–node–metastases classification scheme for staging.⁶ The requirement for "grossly visible" involvement of venous channels including "segmental (muscle-containing) branches" for stage T3b seems illogical, as this is a function of the care with which dissection and gross examination of the renal sinus are performed, rather than the biological stage of the tumour. We suggest a definition based on intraluminal growth of tumour, whether identified macroscopically or microscopically (fig 1).

The second problem is the lack of clarity in the RCPATH minimum dataset. A recommended dissection protocol, a requirement to record the presence or absence of RSVI and recommendations about numbers of blocks to take (eg, 10

initially and additional blocks if no RSVI is identified histologically) could be provided in the next version.

We describe here the second and, to date, the largest prospective study of a novel cut-up protocol for nephrectomy

Figure 1 Suggested classification of renal sinus vein invasion (RSVI). The earliest stage (A) is destruction of the muscular wall of the vein (shown in red in the schematic) with the tumour (shown in yellow in the schematic) covered only by endothelium. This is followed by intraluminal expansion of the tumour (B) and finally extension along the vein away from the main tumour (C). In this study, RSVI was defined as those cases in which at least stage B could be shown histologically. Corresponding examples of haematoxylin and eosin-stained sections from the tumour–renal sinus interface from cases of renal cell carcinoma are shown opposite the schematics.

Take-home messages

- A new protocol for the dissection of nephrectomy specimens for renal cell carcinoma was devised in Cardiff, UK, in order to assess vascular invasion more effectively.
- Introduction of this protocol in Oxford significantly increased the detection of vascular invasion in the renal sinus, thus increasing the number of tumours staged as T3b, while causing only a small increase in workload.
- We suggest widespread introduction of this protocol, its inclusion in the Royal College of Pathologists' Minimum Dataset for renal tumours and further clarification of exactly which type of vessel must be invaded for tumours to be staged as T3b.

specimens for RCC^{4 5} and show markedly increased detection of vascular invasion, with only a small increase in laboratory workload.

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