Renal nuclear medicine: can it survive the millennium?

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The reflex use of nuclear medicine investigations by nephrologists reflects its relative safety but fails to take account of either the value or the comparative expense of these tests. This editorial re-examines the contribution of isotopic renography to clinical management.

Assessment of renal function and structure

Isotopic renograms can provide information about dynamic function and structure depending on the handling of the radioisotopes which are either filtered at the glomerulus, (EDTA and DTPA), or extracted and secreted by the tubule, (HIP, MAG3 and DMSA).

Both EDTA and the modern formulations of DTPA, which are minimally protein-bound, can be used to measure glomerular filtration rate (GFR) [1]. The accuracy improves as the number of plasma samples and the duration of the sampling period is increased, although DTPA is less reliable than EDTA when the GFR is less than 30 ml/min. DTPA renography should routinely measure GFR as well as providing a dynamic image and split function.

The 99technetium labels, usually DTPA or MAG3, provide the best dynamic images, with MAG3 preferred in renal insufficiency. Renal structure is best defined by 99technetium-DMSA (a static tracer) with computer enhancement able to generate tomographic

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The diagnosis but not the exclusion of obstruction

Although ultrasound can demonstrate pelvicalyceal dilatation, this does not always mean obstruction and the diuresis renogram is widely used to diagnose or exclude outflow tract obstruction. It is less sensitive than the Whittaker test (antegrade nephrostogram) in which outflow tract pressures are measured directly. This is partly due to the failure to adhere to consensus guidelines on methodology [9], in particular those regarding the timing of diuretic dose and the state of the patient’s hydration, since exclusion of obstruction requires the kidney to generate a high urine flow rate (>10 ml/min). False positive tests may occur when the renal pelvis is capacious, if there has been previous pyeloplasty, if only supine images are taken or if a ureteric stent is present. Bladder distention can cause functional vesicoureteric junction (VUJ) obstruction and conversely, in patients with proven pelvi-ureteric junction obstruction, concomitant VUJ obstruction can be missed. Only some of these confounding factors are avoidable and when eliminated, diuresis renography can strongly suggest the diagnosis of obstruction but the definitive exclusion of obstruction may still require an invasive study.

The exclusion but not the diagnosis of renovascular hypertension

Maintenance of the GFR in patients with renal hypoperfusion depends on improved efferent arteriolar tone mediated by angiotensin II. This provides the basis for angiotensin converting enzyme (ACE) inhibitor renography in which renograms of an adequately hydrated patient are performed before and then after ACE inhibition (usually with oral captopril, 25 mg). This test is used to screen patients with suspected renovascular hypertension and demonstrates a high level of specificity when compared with the gold standard of renal angiography. But as with the diuresis renogram, failure to achieve a consensus with the methodology has limited its sensitivity [10], reduced in any case by a recent meal, hypovolaemia, recent therapeutic administration of an ACE inhibitor and the presence of bilateral disease. The sensitivity of the ACE inhibitor renogram must also depend on the degree of renal artery stenosis but surprisingly this relationship has not been specifically defined.

So, a normal captopril renogram makes a diagnosis of unilateral renovascular hypertension extremely unlikely and given that an abnormal renogram is also a sensitive predictor of the success of subsequent angioplasty in treating hypertension, further intervention (such as angiography) can reasonably be spared [11]. The use of captopril renography in patients with renal failure secondary to renovascular disease and the prediction of a useful response to intervention, let alone its safety in these patients [12], remains unvalidated.

The diagnosis of acute renal failure

Ultrasound can measure renal size, exclude bilateral obstruction and Doppler ultrasound will exclude a vascular catastrophe. Aside from hypeerechoic images present in cast and HIV nephropathy, ultrasound fails to differentiate between acute tubular necrosis, acute glomerular disease and acute interstitial nephritis. Despite the ubiquitous use of DTPA or MAG3 renography in patients with acute renal failure, neither diagnostic nor prognostic benefit has been reported and there is certainly no evidence that repeat scans are more helpful to the clinician than serial measurements of urinary volume and creatinine content.

The renal transplant

Following renal transplantation, renography is frequently undertaken to confirm perfusion, but makes no contribution to the management of the immediately functioning transplant with a single artery. Acute renal dysfunction can result from acute tubular necrosis, rejection or cyclosporin toxicity and renal biopsy remains the definitive diagnostic test. Early reports suggested that perfusion and uptake indices could not differentiate between cyclosporin nephrotoxicity and rejection, but subsequent investigators have used deconvolution techniques to analyse outer and middle zone transit times separately in patients with biopsy-proven dysfunction and can differentiate acute rejection from other causes of parenchymal dysfunction [13,14]. Even if the sensitivity and specificity of this technique is improved, it is unlikely to supplant biopsy given the importance of an unequivocal diagnosis.

Baseline dynamic renograms are not helpful but if performed must be delayed until renal transplant function is stable and the ureteric stent (if used) removed. Subsequent routine renography is also non-contributory except for special patient groups such as those with urinary diversions to exclude late distal ureteric stenosis. Protocols to investigate transplant dysfunction commonly include dynamic renography to exclude obstruction and previous comments regarding renal function and methodology apply. In patients with abnormal lower tracts, DMSA renography can help to differentiate between graft dysfunction due to cortical scarring secondary to recurrent infection and chronic rejection [15].

The superficial nature of the pelvic renal transplant makes Doppler ultrasound the most sensitive (and safest), although not the most specific, non-invasive technique to diagnose renal artery stenosis [16]. Interestingly, as with native kidneys, captopril renography may have a prognostic role for renovascular intervention in patients with new or poorly controlled hypertension [17].
Summary

Much of the progress in renal nuclear medicine has been driven by technological development, but without rigorous assessment the value of some of these studies has been overestimated. The only tests to achieve gold standard status are the isotopic GFR, the DMSA renogram to detect cortical abnormalities and the captopril renogram when used to define those hypertensive patients who will not benefit from renovascular intervention. Consensus guidelines must be followed and routine protocols for combination tests must be developed, but even so isotopic renography is likely to be overtaken by competing technologies which can provide one test to give simultaneous information about both structure and function.

References

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An opportunity to intervene: erythropoietin for the treatment of anaemia in pre-dialysis patients

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Historical perspective

Bright documented the association of anaemia with renal failure in 1836. However, the cause of anaemia was not understood until Erslev, in 1953, identified a hormone that regulated erythropoiesis [1]. Jacobson et al. [2] subsequently established that the kidney produced this hormone termed erythropoietin (EPO). Miyake and colleagues [3] purified human urinary EPO in 1977, making it possible to clone the EPO gene and initiate clinical trials of EPO for the treatment of anaemia in renal failure. EPO has proven to be of

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