Is it practical to screen dialysis patients for vascular calcification?

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Introduction

Vascular calcification is becoming increasingly appreciated as an important risk factor for cardiovascular morbidity and mortality in chronic kidney disease (CKD) patients who are receiving dialysis therapy. Calcification of coronary arteries and peripheral conduit arterial vasculature is highly prevalent [1] in both haemodialysis (HD) and peritoneal dialysis (PD) patients, although most studies up to now have focused on HD [2,3]. These structural changes are associated with significant functional disturbance, chiefly resulting in reduced arterial compliance [4]. Reduction in arterial compliance increases the pulse wave velocity and predisposes to demand myocardial ischaemia [5], especially when combined with the characteristic ‘phenotype’ of the chronic dialysis patient, which includes a high incidence of epicardial coronary artery disease, small vessel myocardial disease and increased left ventricular mass, all predisposing to myocardial ischaemia. Moreover, vascular calcification with associated reduced arterial compliance is associated with reduced baroreflex sensitivity (BRS), and further dysregulation of short-term blood pressure (BP) control during HD [6].

The high prevalence, functional significance and progressive nature (over a relatively short time span) of vascular calcification suggests that detection and surveillance may be worthwhile in general clinical practice. This would allow more accurate risk stratification and monitoring of therapeutic strategies designed to abrogate or potentially regress vascular calcification. In this edition of NDT, Taniwaki and co-workers report a semi-quantitative cross-sectional study of aortic calcification in 667 HD patients, using conventional abdominal CT scanning [7]. This further raises the possibility of assessing vascular calcification in HD programme as a whole, and consideration of which of the currently available techniques might be potentially best utilized to perform this.

Ultrasound based methods

Ultrasound based methods have been widely utilized in this patient group. This is typically used to study the carotid artery [8]. Vessel calcification can be imaged and additional functional parameters assessed. The measurement of common carotid artery incremental elastic modulus has been reported to correlate well with aortic PWV, and was also predictive of subsequent cardiovascular and all cause mortality in a long-term prospective study [4]. Ultrasound relies on proven universally available technology, which is relatively inexpensive. It also does not require exposure to ionizing radiation (a potential benefit if long-term surveillance is being considered). There are, however, a number of drawbacks to using it in general clinical practice. The measurements required to study vascular calcification require a skilled and consistent operator, the approach so far has been robustly assessed only in combination with plain radiological assessment of multiple arterial sites and it is unable to differentiate medial from intimal calcification (a common feature of all the currently applicable methods). A more significant limitation is that, although ultrasound provides a relatively sensitive tool for the detection of carotid vascular calcification, the data derived are qualitative and are unlikely to be sufficiently sensitive to track changes, at least over the shorter term. Ultrasound though remains the only readily available technique capable of imaging uncalcified plaque. Furthermore, a new generation of higher resolution ultrasound machines (not currently widely available) allows high-precision measurement of plaque thickness and volume. This greater spatial resolution and the ability

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to correlate these appearances with ultrasound derived functional measures (such as distensibility index) will allow more accurate quantitative assessments (although only at arterial sites readily accessible to ultrasound).

Plain radiology

Plain radiology of pelvis, thigh or hands has been utilized in a number of studies of vascular calcification. It is the approach that has been most extensively studied and best correlated with both arterial compliance measures and patient events/survival [9]. Furthermore, it is the only technique for the detection of vascular calcification included in the NKF-DOQI clinical practice guidelines for cardiovascular disease in dialysis patients. Progressive calcification has been reported using this approach, but only in a retrospective study [10]. The limitations of observer-dependent scoring systems and the detection sensitivity of plain radiology itself again yield only semi-quantitative data that is likely to be unsuitable to accurately track changes in calcification status. The pattern of calcification on plain radiographs (linear vs irregular calcification) yields some information concerning the balance between medial and intimal vascular calcification [9]. The presence of predominantly linear calcification (implying medial calcification characteristically seen in this patient group) has been demonstrated to be associated with a significant increase in cardiovascular risk. However, full discrimination between these often co-existing entities and the importance of this distinction is still a matter of further study.

Electron beam computed tomography (EBCT)

EBCT is a highly sensitive method for detecting vascular calcification [11]. Subsequent assessments (at multiple sites) of calcification density and volume allow quantitative scoring of vascular calcification to be performed. EBCT has largely been applied to coronary arteries, but data on proximal intrathoracic aortic calcification are also usually available. Due to ECG gating during image acquisition, the exposure to ionized radiation is relatively low.

EBCT has been successfully used to study prevalent and progressive vascular calcification, as well as the impact of therapy (sevelamer vs calcium-based phosphate binder medication) [12]. Calcification scores derived from EBCT correlate with arterial compliance, as measured by aortic PWV [13]. Studies of vascular calcification and cardiovascular outcomes are yet to be performed, and controversy exists concerning the correlation of coronary artery calcification scores and the angiographic appearances [14,15]. The scoring requires the area of interest to be manually delineated, and therefore the process does have a degree of operator dependability. The main limitations for the widespread use of EBCT are the scarcity of suitable scanners and attendant cost implications.

Other computed tomography (CT) techniques

Modern 8 and 16 slice spiral CT scanners have been used to study vascular calcification at a variety of sites in patients on HD and PD. The technique has been used to generate coronary artery calcification (CAC) scores analogous to those from EBCT (using a conventional scanner but with specialized software) [16,17]. This relies however on multiple images being taken and retrospective ECG-gating, with most of the images being disregarded. This results in radiation exposure being 3- to 4-fold greater than EBCT. This may be significant if multiple assessments over long periods of time are considered. The limitations for CAC scores obtained in this way are similar to those from EBCT. This approach has also been far less extensively tested than EBCT calcification scoring, but appears to be as robust.

Conventional CT may be used to evaluate non-coronary vascular calcification. Non-contrast CT scans have been used in several studies to assess aortic calcification. The proportion of aortic circumference showing calcification can be used to generate an aortic calcification index (ACI) as a marker of vascular calcification burden. Higher ACI values have been associated with increased levels of inflammatory markers associated with atherosclerosis [18,19]. It is this method that Taniwaki and co-workers have applied in the largest cross-sectional study of vascular calcification in HD patients yet reported [7]. This appears to be a simple and relatively inexpensive method to sensitively detect the presence of aortic calcification, and certainly useful for initial diagnosis. Aortic calcification studied this way correlated with brachial pulse pressure, an indirect marker of arterial compliance (detailed measurement was beyond the scope of this study). Such a method is robust and easily applicable to most chronic HD programmes. Limitations though remain in terms of the ability to accurately quantify the calcification load (or medial/intimal distribution) and therefore track changes. Furthermore, the method has yet to be fully correlated with arterial compliance measurements or cardiovascular outcomes.

Spiral CT can also be applied to other peripheral conduit arteries and to measure calcification scores at the chosen site. Our group has utilized a protocol based on high-resolution scanning of a standardized 6 cm portion of the superficial femoral artery in a prospectively studied group of 134 CKD patients [20]. This technique offers high sensitivity, quantitative scoring, low ionizing radiation exposure and short scan times (typically around 5 min). We have been able to correlate vascular calcification measured by this method with arterial compliance, measured by aortic PWV. This correlation is seen in patients with CKD 4 and CKD 5 (on HD and PD) [21]. Furthermore, this correlation is seen at baseline study and between the change in vascular calcification and PWV over a 1 year period.

Outcome data though are still not available using this modality of assessment. Ideally vascular calcification...
would be evaluated in the exact portion of the circulation being assessed for arterial compliance. However, approaches based on multiple assessment of peripheral arterial calcification have been successfully utilized in the study of arterial compliance and clinical outcomes, and widespread adoption is contingent on pragmatic application of widely available existing techniques.

Further developments in multi detector row spiral CT scanners resulted in the introduction of 32 and 64 slice machines. The increased spatial resolution of these devices may allow subsequent discrimination between medial and intimal calcification, although this is yet to be formally studied.

**Conclusion**

A variety of methods allowing sensitive detection of functionally relevant vascular calcification are currently available. Up to now much of the prospective study of vascular calcification and its consequences has been using approaches based on combinations of techniques. Undoubtedly, this has generated crucial insights into this clinico-pathological entity and a further combined approach using echocardiography (to assess valve calcification), plain radiology (to assess vascular calcification) and pulse pressure as a measure of aortic stiffness has been proposed for widespread adoption for clinical practice (although such an approach has not yet been evaluated in prospective study) [22]. However, the requirements for a successful ‘screening’ method, which include a sensitive reproducible method with low false-positive and false-negative rates, cost effectiveness, ready availability and ease of use, somewhat militate against a strategy based on the integration of information from multiple assessments. A simpler single assessment would appear attractive. Semi-quantitative assessment with plain radiology of multiple arterial sites or CT of the aorta (and ACI measurement) offers sensitive detection of vascular calcification. More sensitive quantification with scoring of coronary or peripheral arterial calcifications is currently practical with readily available multi-slice CT scanning. The clinical utility of such an approach awaits further specific prospective study. However, given that modification of vascular calcification as a cardiovascular risk factor is likely to become an increasingly important aspect of the overall management of CKD patients, a suitable, readily applicable and well-validated method to stratify patients to differing therapies (and monitor response) remains an urgent priority.

Conflict of interest statement. None declared.

(See related article by Taniwaki et al. NDT 20: 2472-2478 and McIntyre et al. NDT Advance Access: Nov. 1 2005, doi: 10.1093/ndt/gfi236)

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Arteriovenous fistula after renal transplantation: utility, futility or threat?

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Introduction

Creation of an arteriovenous (AV) fistula for haemodialysis therapy provides convenient access to the circulation in patients with end-stage renal disease. However, the chronic volume overload induced by the AV fistula induces structural and functional cardiac changes, including left ventricular remodelling, which may be deleterious. The balance between the need for vascular access and the deleterious effects of a patent AV fistula on cardiac function and morphology obviously favours the former in patients requiring long-term haemodialysis. After renal transplantation, however, the value of keeping an AV fistula patent is more uncertain and whether it should be closed after successful renal transplantation remains a matter of debate. Since recent studies have provided more insight into the cardiac and haemodynamic changes induced by the procedure, this review aims to summarize the pros and cons of AV fistula closure.

Determinants of left ventricular morphology after renal transplantation

Left ventricular hypertrophy is highly prevalent among patients with end-stage renal disease [1]. Hypertension and chronic anaemia appear to be the main stimuli for the development of left ventricular hypertrophy in dialysis patients, although age, diabetes and metabolic factors may also play a role. Left ventricular dilatation is also frequent and is associated with anaemia, hypertension, hypoalbuminaemia, ischaemic heart disease and plasma volume expansion [2]. In addition, left ventricular adaptation to the chronic volume overload induced by AV fistulas is characterized by increased stroke volume and cardiac output and by left ventricular enlargement; the resulting left ventricular hypertrophy is predominantly eccentric (i.e. characterized by increased left ventricular mass with normal relative wall thickness) [2,3]. Renal transplantation improves left ventricular volume, paralleling the correction of uraemia and volume status, the normalization of the haemoglobin level and the rise in serum albumin and may reduce left ventricular hypertrophy [4,5]. However, the prevalence of left ventricular hypertrophy remains high, with uncontrolled hypertension and anaemia as main contributing factors. Strict blood pressure control contributes to the regression of left ventricular hypertrophy [6]. The effect of a patent AV fistula on left ventricular morphology after renal transplantation had received little attention until recent data suggested a significant contribution to residual hypertrophy [7–11].

Deleterious effects of AV fistulas

Complications of AV fistulas are not uncommon and include steal syndrome, arm oedema, thrombosis and, rarely, traumatic bleeding. Furthermore, patients frequently consider the presence of a dilated and