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Original Article

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Association of pelvic arterial calcification with arteriovenous thigh graft failure in haemodialysis patients

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Abstract

Background. Arterial calcification is a common problem in patients with chronic kidney disease, and has been associated with adverse clinical outcomes. The goal of the present study was to evaluate whether pelvic artery calcifications are associated with technical failure of arteriovenous thigh grafts in haemodialysis patients.

Methods. From 1 January 1999 to 30 June 2002, thigh grafts were placed in 54 haemodialysis patients who had exhausted all options for permanent vascular access in the upper extremities. Perioperative computed tomography (CT) of the abdomen and pelvis was obtained in 32 of the patients for diagnostic purposes unrelated to vascular access planning. Two radiologists, who were blinded to the graft outcomes, scored the vascular calcifications on CT of the distal aorta, common iliac, external iliac and common femoral arteries on a semi-quantitative 5-point scale. The association between technical graft failure (inability to complete the anastomosis) and the vascular calcification score was analysed.

Results. There was a high inter-observer agreement in scoring vascular calcification ($\kappa = 0.801$). Among 26 patients with absent or mild pelvic arterial calcifications (grade 1–2) on CT, none (0%) experienced technical graft failure. In contrast, three of six patients (50%) with moderate to severe calcification (grade 3–5) had technical graft failures ($P = 0.004$ by Fisher's exact test). The cumulative 1 year graft patency was lower in the group with grade 3–5 calcification (33 *vs* 81%, $P = 0.09$). The two groups were similar in age, gender, race, diabetes, duration of dialysis, serum calcium, serum phosphorus and serum parathyroid hormone.

Conclusion. There is a strong association between pelvic artery calcifications and technical failure of thigh grafts. The presence of moderate to severe vascular calcification is predictive of poor cumulative 1 year graft patency.

Keywords: dialysis shunts; graft; Doppler ultrasound; haemodialysis; vascular calcification

Introduction

Arterial calcification is observed commonly in patients with chronic kidney disease [1], and may affect coronary, carotid and peripheral arteries [2–6]. Vascular calcification has been associated with adverse clinical outcomes in haemodialysis patients, including ischaemic cardiac events, claudication and mortality [5,6]. Intimal calcification leads to vascular thrombosis, whereas medial calcification produces vascular stiffening [7]. Peripheral vascular disease is much more common in dialysis patients than in the general population [8,9]. Moreover, graft and limb patency following peripheral bypass surgery is far inferior in dialysis patients, as compared with those having normal renal function [10]. Vascular calcification may contribute to the severity of peripheral artery disease in dialysis patients [11].

It is not known whether vascular access outcomes in haemodialysis patients are associated with arterial calcification. In the subset of haemodialysis patients who have exhausted all options for permanent vascular access in the upper extremities, an arteriovenous synthetic graft is often placed in the thigh. The large diameter of the femoral vessels would suggest an excellent technical outcome of thigh grafts. To our surprise, we recently observed that the frequency of technical failure (inability of the surgeon to perform the anastomosis) was twice as high for thigh grafts, as compared with upper extremity grafts [12]. Review of the operative notes revealed the presence of severe arterial calcification precluding successful surgical femoral artery anastomosis to the graft in most patients with technical failures.

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The goal of the present study was to evaluate retrospectively whether the magnitude of pelvic arterial calcifications measured in perioperative radiological studies correlated with the likelihood of technical failure of thigh graft placement.

Methods

Patient population

This clinical study was performed with the approval of our Institutional Review Board. Using a prospective, computerized vascular access database at our institution [13], we identified 63 thigh graft placements in 54 patients during the 3.5 year period from 1 January 1999 to 30 June 2002. Only the initial thigh graft was included for analysis for patients receiving two thigh grafts during the study period. The technical outcomes of the graft placements were known in all 54 patients.

Graft technique and evaluation of outcomes

All A-V graft procedures were performed by one of three experienced Transplant Surgeons. The patients were evaluated by the surgeons for evidence of peripheral vascular disease. If peripheral vascular disease was suspected clinically, non-invasive studies were obtained. If there was a clinical suspicion of moderate or severe peripheral vascular disease, a thigh graft was not placed. In suitable patients, a PTFE (polytetrafluoroethylene) graft was anastomosed to the greater saphenous vein or common femoral vein, and then looped subcutaneously in the upper thigh and anastomosed to the femoral artery. Graft placement outcomes were obtained from the prospective dialysis database. Technical failure of graft placement was defined as inability of the surgeon to complete the graft anastomosis and obtain a patent graft at surgery.

Radiological vascular calcification scoring

Radiological studies are not obtained for pre-operative evaluation prior to thigh graft placement at our institution. However, using the hospital Radiological Information System, we identified 32 patients with thigh grafts who received CT scans of the abdomen and pelvis for unrelated diagnostic purposes during the time period surrounding the thigh graft placement. The median time between the CT scans and the thigh graft surgery was 213 days. These CT scans were used to grade the severity of pelvic arterial calcification in the study population. Most of the patients were evaluated by CT using a Lightspeed or CTi scanner (GE Medical Systems, Milwaukee, WI). The routine abdominal and pelvic CT used 5 mm axial images at 10 mm increments through the pelvis. Oral and intravenous contrast was given based on the clinical indication for the study. Patients without adequate radiological studies to grade the arterial calcification were excluded from this analysis.

Two radiologists with abdominal imaging specialization (M.E.L. and M.M.M.), who were blinded to the patients' clinical information and thigh graft placement outcomes, independently graded each CT scan for calcifications involving the distal aorta, common iliac arteries, external iliac arteries and common femoral arteries. Among patients with asymmetric involvement of bilateral arteries, the more severely involved side was used for analysis, since the reviewers did not know the side of graft placement. The overall severity of calcification was graded semi-quantitatively using a 5-point scale, ranging from absent or minimal calcifications to severe diffuse calcifications using the following criteria. (i) Grade 1: either (a) no arterial calcifications from the distal aorta to the common femoral arteries, or (b) minimal non-circumferential non-contiguous scattered arterial calcifications without 50% circumference involvement of any segments. (ii) Grade 2: mild non-circumferential non-contiguous arterial calcifications involving numerous segments with <50% involvement of most individual segments. Isolated non-contiguous images with >50% calcification may be present, but no areas of completely concentric vascular calcification. (iii) Grade 3: moderate non-circumferential non-contiguous calcifications of multiple arterial segments with >50% calcification of multiple segments, but without any completely concentric calcification of the arteries. (iv) Grade 4: moderate calcifications involving multiple segments of arteries with most areas having >50% involvement with calcification. Isolated completely concentric calcifications may be present. (v) Grade 5: diffuse calcifications with multiple levels of completely concentric calcifications.

Representative examples of CT scans with high and low calcification scores are shown in Figures 1 and 2.

Clinical and laboratory data

A nephrologist (M.A.) reviewed each patient's medical records. Information on patient demographics, diabetic status and duration of dialysis prior to thigh graft placement was extracted. In addition, laboratory values including monthly biochemical profiles and quarterly serum parathyroid hormone (PTH) levels closest to the surgery date were recorded. Biochemical data collected included serum calcium, phosphorus, intact PTH, calcium × phosphorus product and alkaline phosphatase.

Statistical analysis

Cohen's κ test for an ordinal scale [14] was performed to evaluate inter-observer variability between the two blinded radiologists scoring the arterial calcifications in the CT scans. The association between technical thigh graft failure and vascular calcification score was evaluated using Fisher's exact test. Comparison of clinical and laboratory measurements between the groups with the high and low calcification scores was performed by χ^2 test, unpaired Student *t*-tests and non-parametric Mann–Whitney tests, as appropriate. A *P*-value <0.05 was considered statistically significant.

Results

Thirty-two patients who underwent thigh graft surgery, and had CT studies suitable for scoring pelvic arterial calcifications, were included in this study. The mean age of the study population was 52 ± 14 years (range 29–79 years). This patient population included 53% females, 94% blacks and 28% diabetics.

Fig. 1. Representative non-contrast CT images of the pelvis in a 53-year-old patient with mild arterial calcification, grade 1, who had successful thigh graft placement. (**a–c**) Only scattered <50% circumference calcifications are present in the distal aorta (arrowheads), common iliac (arrows) and common femoral arteries (curved arrows). (**d**) No calcifications were detected in the external iliac arteries (thick arrows).

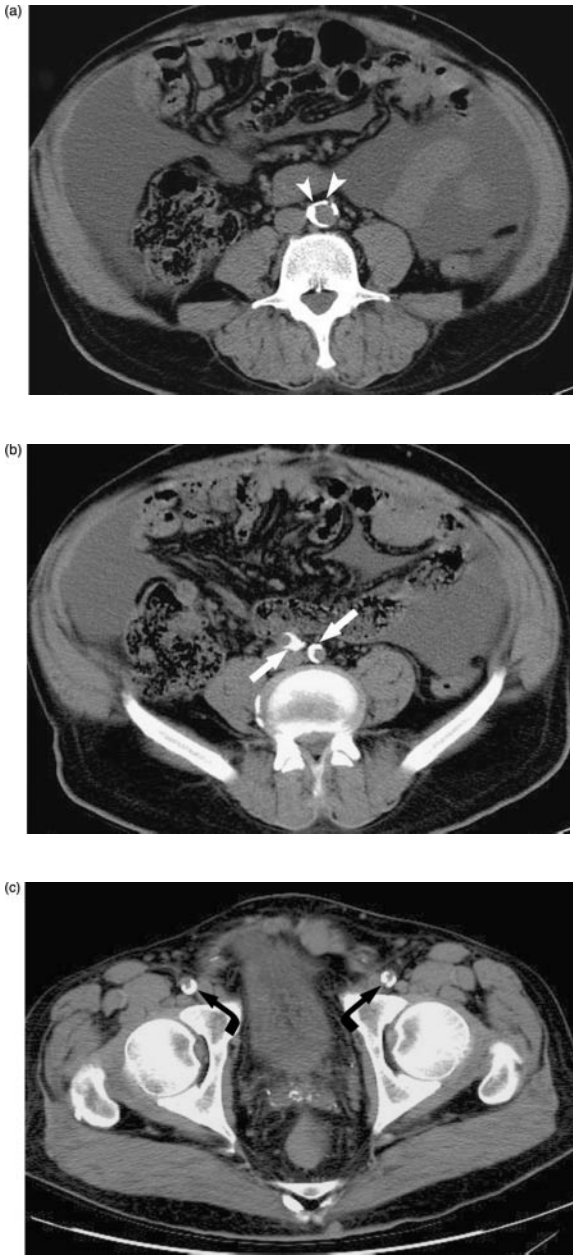

Fig. 2. Representative non-contrast CT images of the pelvis in a 51-year-old patient with severe arterial calcifications, grade 5, in whom a thigh graft was unsuccessful at surgery. (**a–c**) Note the concentric dense calcifications in the distal aorta (arrowheads), common iliac arteries (arrows) and common femoral arteries (curved arrows).

The inter-observer coefficient of agreement on calcification scores between the two blinded radiology observers was high, with a weighted κ value = 0.801, indicating substantial to near-perfect agreement. Because only five of the 32 CT scans were assigned intermediate calcification scores (2, 3 or 4), we divided the patients into two groups: those with low calcification scores (1–2) and those with high calcification scores (3–5). The two observers agreed on the classification of patients into the low or high calcification group in 31 of 32 (97%) cases.

Among the patients with a low calcification score (grade 1–2), none of 26 (0%) patients had a technical failure of thigh graft placement. In contrast, three of six (50%) patients with moderate to severe vascular calcification (grade 3–5) experienced a technical failure in graft placement ($P = 0.004$, Fisher's exact test). The cumulative thigh graft survival (from initial surgery to permanent failure) at 1 year was 33% in the high calcification group, as compared with 84% in the low calcification group ($P = 0.09$). Pelvic artery calcifications were generally most severe in the internal iliac arteries, but these arteries were not considered in the grading algorithm, because of our previous clinical experience suggesting that internal iliac calcifications were more prevalent even in patients with less severe arterial calcific disease. The next most severely calcified arteries were typically the common femoral arteries and the common iliac arteries. There were symmetric calcifications involving the common femoral arteries of at least 50% circumference in each lower extremity in all patients with moderate to severe calcifications.

Patients with severe vascular calcifications were more often male and older, and less often diabetic, but none of these differences reached statistical significance (Table 1). The duration of dialysis was similar between the two groups. Serum calcium levels tended to be higher among patients with higher calcification scores than those with low scores. The serum phosphorus, PTH, calcium × phosphorus product and serum alkaline phosphatase levels were similar between the two patient groups.

The six patients with high vascular calcification scores were subcategorized into two groups: those with technical graft failures and those with technical successes. The small number of patients ($n = 3$ per subgroup) precludes meaningful statistical comparisons. None of the patients was receiving anticoagulation. The operative reports in the first group documented severe calcification of the femoral artery, that precluded performing an anastomosis. All three patients received a tunnelled dialysis catheter for long-term haemodialysis. In the operative reports of the subgroup with successful thigh graft creation, there was no mention of vascular calcification. The subgroup of patients with technical graft failures tended to have a longer duration of dialysis, as well as higher serum intact PTH, phosphorus, calcium × phosphorus product and alkaline phosphatase (Table 2). All these differences would favour more diffuse arterial calcification.

Table 1. Patient characteristics based on severity of calcifications

Parameter	High calcification score (3–5)	Low calcification score (1–2)	*P*-value
Age (years)	55 ± 10	51 ± 15	0.51
Gender (% male)	67	42	0.28
Diabetes mellitus (%)	17	31	0.49
Duration of dialysis (years)	4.9 ± 2.2	4.1 ± 4.6	0.72
Serum calcium (mg/dl)	9.6 ± 0.4	8.7 ± 1.1	0.08
Serum phosphorus (mg/dl)	6.3 ± 1.6	5.8 ± 2.0	0.62
Ca × P product (mg^2/dl^2)	60 ± 14	50 ± 19	0.30
Serum alkaline phosphatase (U/l)	157 ± 91	122 ± 79	0.39
Serum intact PTH (pg/ml)	908 ± 797	665 ± 936	0.59

Values are means ± SD.

Table 2. Comparison of the high calcification patient subgroups with technical graft failure *vs* technical graft success

Parameter	Technical failure	Technical success
Duration of dialysis, years	5.9	3.4
Serum calcium (mg/dl)	9.6	9.6
Serum phosphorus (mg/dl)	6.9	5.2
Ca × P product (mg^2/dl^2)	66	50
Serum alkaline phosphatase (U/l)	203	88
Serum intact PTH (pg/ml)	1146	552
Haemoglobin (g/dl)	11.1	9.5
Leukocyte count	6700	6700
INR	1.05	0.97

Values are means. Statistical comparisons not performed due to the small number of patients.

Discussion

Dialysis patients frequently have vascular calcification [1]. Goodman *et al*. [2] reported an 88% prevalence of coronary artery calcification among dialysis patients aged 20–30 years. The severity of calcification correlated with patient age, number of years on dialysis and calcium intake. Moreover, serial studies documented progression of the calcification in a subset of patients. Oh *et al*. [3] confirmed these findings and also observed frequent calcification of carotid arteries. Chertow *et al*. [4] documented an increase in the calcification scores of coronary arteries and thoracic aortas in haemodialysis patients ingesting calcium-containing phosphate binders for 1 year. Coronary artery calcification has been associated with coronary atherosclerosis both in patients with normal kidney function [15] and in haemodialysis patients [6]. Arterial calcification is also associated with aortic stiffness, which in turn predicts decreased survival in dialysis patients [5,16].

Peripheral arteries are also frequently calcified in dialysis patients [11]. The present study documents that moderate to severe calcification of the pelvic arteries is clinically significant, in that it frequently precludes successful construction of an arteriovenous thigh graft. Since these patients have already exhausted all options for permanent vascular access in the upper extremities, they will need to dialyse permanently with tunnelled dialysis catheters. Dialysis catheters are inferior to grafts in several respects. They become thrombosed and infected more frequently, and provide lower dialysis blood flows [17]. Moreover, catheter-dependent dialysis patients have

more frequent infection-related hospitalizations and deaths [18–20].

The aetiology of the severe pelvic artery calcification in our study is not clear. Patients with moderate to severe calcifications did not differ from those with absent or mild calcification in age, years on dialysis or frequency of diabetes. The two groups were also similar in biochemical markers of bone disease. It is possible that the patients with severe arterial calcification had a greater cumulative intake of oral calcium-based phosphate binders, but this could not be ascertained because of the retrospective nature of this study. The magnitude of vascular calcification may be affected by novel calcification inhibitors, such as matrix Gla-protein (MGP) and fetuin-A [7]. Warfarin, an inhibitor of MGP, may increase arterial calcification [7], but none of our patients in the high calcification group were anticoagulated.

The present study had several limitations. First, its retrospective nature could introduce potential biases in data analysis. However, it should be noted that a prospective, computerized database was used to identify all thigh graft procedures and their surgical outcomes, thereby ensuring a complete list. It is also possible that the subset of patients for whom perioperative CT scans were available differed from those patients missing such an evaluation. Even at our large dialysis centre (~500 haemodialysis patients), only ~15 patients received a thigh graft each year. Thus, duplicating the present study prospectively would require several years.

Secondly, we used a semi-quantitative calcification scoring system that was somewhat subjective, in contrast to previous studies that quantified calcification using electron beam CT [2–4]. However, the arterial calcification scores were determined by radiologists specialized in reading abdominal imaging. Moreover, the two observers were blinded to the clinical information on the patients and their thigh graft outcomes, precluding unconscious bias in scoring. Finally, there was a high degree of agreement between the two observers.

Thirdly, the CT scans used to score vascular calcification were not obtained specifically for surgical vascular access planning, and the median interval between the CT scan and thigh graft placement was 213 days. It should be noted, however, that 84% (27 out of 32) of the patients were in the least severe or most severe calcification categories. This means that the difference in arterial calcification between patients with successful and unsuccessful graft placement was striking. While it is possible that arterial calcifications may have progressed or regressed slightly in the time interval between the radiological study and the thigh graft surgery, it is extremely unlikely that patients would progress from minimal to severe calcification in such a brief time period.

In conclusion, the presence of moderate to severe pelvic arterial calcifications is strongly associated with technical failures of haemodialysis grafts placed in the thigh. However, a thigh graft was placed successfully in three of six patients in the high calcification group, suggesting the possibility of non-uniform arterial calcification that is not apparent on the CT scan. Given that the alternative to a thigh graft is long-term dialysis with a tunnelled catheter, it may still be reasonable to attempt a thigh graft in such patients, while recognizing that about half of these attempts will be unsuccessful.

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Conflict of interest statement. None declared.

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