American Journal of Transplantation 2005; 5: 1689–1693
Blackwell Munksgaard

doi: 10.1111/j.1600-6143.2005.00914.x

Early Subclinical Coronary Artery Calcification in Young Adults Who Were Pediatric Kidney Transplant Recipients

Michael B. Ishitani[a,*], Dawn S. Milliner[a], Dean Y. Kim[a], Humberto E. Bohorquez[a], Julie K. Heimbach[a], Patrick F. Sheedy, II[b], Bruce Z. Morgenstern[a], James M. Gloor[a], Joseph G. Murphy[c], Robert D. McBane[c], Lawrence F. Bielak[d], Patricia A. Peyser[d] and Mark D. Stegall[a]

[a] *William J. von Liebig Transplant Center,* [b] *Department of Radiology,* [c] *Division of Cardiovascular Medicine, Mayo Medical School, Foundation and Clinic, Rochester, MN and* [d] *Department of Epidemiology, University of Michigan, Ann Arbor, MI, USA*
* *Corresponding author: Michael B. Ishitani, Ishitani.Michael@mayo.edu*

Coronary artery disease (CAD) is the leading cause of death in adults after successful kidney transplantation. Children who have undergone successful kidney transplantation are entering young adulthood; however, the prevalence and extent of CAD in this population is unknown. We conducted a pilot study in young adults with stable allograft function, who received kidney transplants as children to measure coronary artery calcification (CAC), a marker of coronary artery atherosclerosis and CAD. We evaluated 19 young adults after successful pediatric kidney transplantation for known CAD risk factors; these patients underwent noninvasive imaging with electron-beam computed tomography (EBCT) for measurement of CAC. Prevalence and quantity of CAC were then compared to asymptomatic individuals from the community. All patients had multiple risk factors for CAD. Mean age at evaluation was 32 years (range: 21–48 years). CAC is uncommon in individuals in the community in this age range; however, nearly half of our patients had CAC detected with the quantity of CAC comparable to asymptomatic individuals from the community 10–40 years older. These data suggest young adults who received pediatric kidney transplants are at increased risk for developing early CAC and need close monitoring to detect early CAD so as to prevent premature cardiac morbidity and mortality.

Key words: coronary artery calcification, coronary heart disease, electron beam computed tomography, pediatric kidney transplant

Received 1 October 2004, revised and accepted for publication 16 February 2005

Introduction

Kidney transplantation is the treatment of choice for pediatric patients suffering from end-stage renal disease (ESRD). Since 1988, over 10 000 pediatric renal transplants have been performed in the United States (1). During this time period, the survival rates for both patients and allografts have steadily improved (2–4). As they mature and enter young adulthood, many will have risk factors associated with the development of coronary artery disease (CAD). This is concerning because in adults with a functioning allograft, the most common cause of death is CAD with a cumulative incidence of 23% over 15 years (5).

Coronary angiography remains the current standard for diagnosing the presence and extent of CAD. Angiography, however, is invasive, costly and not without significant morbidity, thereby limiting its use as a screening modality. Recently, electron-beam computed tomography (EBCT) has been used to noninvasively determine the quantity of coronary artery calcification (CAC). CAC is a marker of coronary atherosclerosis and CAD and a direct relationship exists between CAC and both histologic and radiologic measures of atherosclerotic plaque on a heart-by-heart, vessel-by-vessel and segment-by-segment basis (6,7). CAC detected by EBCT has a sensitivity and specificity of 97% and 72%, respectively, to detect $\geq$50% stenosis identified on coronary angiography (8). Presence of large quantities of CAC correlates with the presence of clinically significant CAD (9–11).

Interestingly, Goodman et al. reported large quantities of CAC in over 85% of young adult dialysis patients who underwent EBCT, suggesting that these patients are at risk for the development of early and aggressive CAD (12). Oh et al. studied a mixed population of young adult dialysis and transplant patients (13). They found CAC in 92% of patients, with higher CAC scores among those on dialysis compared to those who were transplanted. Higher CAC scores were positively associated with the length of time patients had been on dialysis.

Our pilot study was conducted among young adults who underwent renal transplantation as children, after having had minimal exposure to dialysis prior to and after transplantation. The aim was to evaluate these young adults for CAD risk factors and for the presence and quantity of CAC detected by EBCT and then to compare these patients to asymptomatic individuals from the community.

Materials and Methods

This study was performed under a protocol approved by the Mayo Foundation Institutional Review Board, Rochester, Minnesota. All patients gave written informed consent. All patients (123 patients) who underwent pediatric kidney transplants performed at the Mayo Clinic, Rochester, Minnesota with long-term allograft function (>8 years) were reviewed. From this group, 19 patients in geographic proximity to our institution and who were continuing their care here were invited at random to participate and entered the study beginning in June 2002 and ending May 2004. All had stable allograft function at the time of evaluation. A medical, social and family history and physical examination were obtained. The patients were then evaluated for clinical and laboratory risk factors for CAD.

Standard clinical laboratory tests were performed on fasting patients on the day of evaluation to determine: serum electrolyte levels, including that of calcium and phosphorus; iothalamate clearance; serum lipid and fractionated lipoprotein levels and C-reactive protein, serum homocysteine and intact parathyroid hormone levels.

The patients then underwent an EBCT [Imatron C-150 EBCT scanner (Imatron, Inc., South San Francisco, California)] examination of the heart. A scan run consisted of 40 contiguous 3-mm thick tomographic slices, from the root of the aorta to the apex of the heart, using 100 ms scan times per tomogram and electrocardiographic gating triggered at end-diastole during 2 to 4 breath-holds.

A radiologic technologist scored the tomograms with an automated scoring system (14). CAC was defined as a hyperattenuating focus within 5 mm of the arterial midline and at least four adjacent pixels in size (i.e. 1.38 mm^2), with CT number above 130 HU throughout the focus. Quantity of CAC was defined as the CAC score developed by Agatston and coworkers (15). All EBCT scans were interpreted by a single experienced radiologist (PFS).

The presence and quantity of CAC were then compared with that observed in an asymptomatic reference population consisting of men and women who participated in the community-based Epidemiology of Coronary Artery Calcification (ECAC) study. In the ECAC study, the tomograms were reviewed by the same radiologist and CAC was measured with the same EBCT scanner, scanning protocol, software package and scoring criteria as in the current study. The ECAC study compiled age- and sex-specific estimates of the prevalence and percentiles for quantity of CAC in asymptomatic men and women aged ≥20 years residing in Olmsted County, MN (16–18). Using these data, the age- and sex-specific probability of having detectable CAC was predicted for each of the 19 patients in the current study. These predicted probabilities were summed for the 19 patients to estimate the number of patients in the study group who would be expected to have detectable CAC. In addition, an 'arterial age' (19) was estimated for each of the 19 patients by comparing their CAC scores with the age- and sex-specific median scores observed in the ECAC study. For example, one male patient age 31 had a CAC score of 42. In the ECAC study, a CAC score of 42 was the median CAC score for men age 58 years. Thus, this 31-year-old man would be estimated to have an 'arterial age' of 58 years, a difference of 27 years from his chronologic age. For patients without detectable CAC, the arterial age was defined as their chronological age.

Results

The characteristics and etiology of renal failure for the 19 patients in this pilot study are shown in Table 1. All patients were white. The mean age at transplant was 14.5 years (range: 5–19 years). Mean age at study evaluation was 32.4 years (range: 21–48 years). Mean follow-up period after transplant was 17.9 years (range: 8–33 years). The majority of patients received preemptive live donor kidney transplants (n = 15) at initial transplantation and never required dialysis. Three patients required short periods of dialysis before transplantation (1 month in one and 6 months in two). Four patients received kidneys from deceased donors. Six patients had a total of nine rejection episodes, and two required antibody therapy. Seven patients underwent retransplantation (two for recurrent IgA nephropathy and five for chronic allograft nephropathy) and four required short periods of dialysis prior to their second transplant (median: 5 months, range: 1–24 months).

Hypertension was found in 15 of 19 patients (8 of 10 without CAC, 7 of 9 with CAC), while hyperlipidemia (elevated serum triglyceride >150 mg/dL or cholesterol >200 mg/dL) was found in 16 of 19 patients (8 of 10 without CAC, 8 of 9 with CAC). Obesity (BMI > 30 kg/m^2) was noted in 3 of 19 and a history of tobacco use in 5 of 19 (1 of 10 without CAC, 4 of 9 with CAC). Only one patient was diagnosed with diabetes mellitus. C-reactive protein was abnormal (>0.800 mg/dL) in 2 of 9 patients with CAC, but none of 10 without CAC. Serum homocysteine was elevated (>13 μmol/L) in 4 of 9 patients with CAC, but also 8 of 10 patients without CAC. Lipoprotein a level was abnormal (>30 mg/dL) in only one patient while intermediate LDL particle size was identified in 4 of 10 patients without CAC and 5 of 9 patients with CAC.

All patients initially received long-term calcineurin inhibitor-based immunosuppression including corticosteroids; two were switched to a rapamycin-based regimen and two were changed to corticosteroids and azathioprine only. Mean corticosteroid dose at the time of evaluation was 6.4 mg/day (range: 4–10 mg/day).

Serum calcium and phosphorus levels were normal in all but one patient and calcium–phosphate product was <45 mg^2/dL^2 in all patients (normal <45.5 mg^2/dL^2). Intact parathyroid hormone level was elevated in 8 of 17 patients (normal <5.2 pmol/L). Mean iothalamate clearance at the time of evaluation was 53.5 mL/min/BSA (range: 17–103 mL/min/SA).

Nine (47%) patients had detectable CAC, while only 2.9 (15%) patients would be predicted to have detectable CAC (Table 1), based on the estimates from the ECAC study. Only patients who were 31 years or older had positive

Table 1: Patient data and CAC score compared to asymptomatic community-based age and sex-matched CAC score

Patient	Sex	Diagnosis	Age atTx	Age at evaluation	Donor	Retransplant	Dialysis	CAC score	Probability of CAC in normal population	Percentile vs. population	Arterial age (years)
1	M	FSGS	5	21	DD	No	No	0	4%	-	-
2	M	Reflux	13	23	Live	Yes/Live	No	0	5%	-	-
3	F	Reflux	8	23	DD	No	No	0	0%	-	-
4	M	GN	11	25	DD	No	Yes (6 months)	0	7%	-	-
5	F	MPGN	18	26	Live	No	No	0	1%	-	-
6	F	GN	19	27	Live	No	No	0	1%	-	-
7	M	Reflux	10	28	Live	Yes/Live	No	0	10%	-	-
8	F	Birth asphyxia	14	28	DD	No	No	0	1%	-	-
9	M	Vasculitis	16	30	Live	No	Yes (1 month)	0	2%	-	-
10	F	Reflux	19	36	Live	No	No	0	4%	-	-
11	M	Reflux	15	31	Live	Yes/DD	Yes (24 months)	42	14%	97%	58
12	M	Hypoplasia	15	33	Live	No	No	138	17%	>99%	65
13	F	MPGN	17	34	Live	No	No	83	3%	>99%	77
14	F	Reflux	16	37	Live	No	Yes (6 months)	60	4%	>99%	76
15	M	Reflux	18	38	Live	Yes/Live	No	103	27%	96%	63
16	F	Familial glom	14	39	Live	No	No	245	6%	>99%	>80
17	M	IgA nephropathy	17	43	Live	Yes/Live	Yes (3 months)	24	39%	80%	55
18	M	Reflux	16	46	Live	Yes/Live	Yes (5 months)	100	47%	88%	63
19	M	GN	15	48	Live	Yes/Live	Yes (1 month)	2200	52%	>99%	>80

DD = deceased donor; FSGS = focal segmental glomerulosclerosis; MPGN = membranoproliferative glomerulonephritis; GN = glomerulonephritis; Familial Glom = familial glomerulosclerosis.
The arterial age is based upon the median CAC score for individuals of the same age and sex based upon data obtained from an asymptomatic normal population (ECAC Study)[16–18]. In patients with no CAC, arterial age is defined as the chronologic age.
Patients 1–10 did not have detectable CAC, patients 11–19 had detectable CAC.

CAC scores. Five patients had CAC scores above the 99th percentile for their age and sex. One patient (CAC score 24, 80th percentile for age and sex) had a subendocardial infarction during the study period. Among those with CAC, the mean difference in individual chronologic age compared to an arterial age based upon the median CAC score observed in asymptomatic ECAC study participants was nearly 30 years (range: 12–43 years). None of the risk factors examined, appeared to have any bearing on the presence or absence of CAC.

Discussion

Data from our pilot study suggest that detectable CAC may be very common in young adults who received kidney transplants as children, and as a result the risk for the development of early aggressive CAD may be high compared to the general population. It is accepted that vascular calcification is a risk factor for the development of clinically relevant CAD in asymptomatic adults and those with chest pain (9–11). Adults with high CAC scores are more likely to have angiographically defined disease as well as histopathologic evidence of disease at autopsy (6–8,20,21). Adults with CAC scores above the 75th percentile have been shown to be at higher risk for future myocardial infarction and coronary death compared with the general population (9–11,22).

It is clear that among adult dialysis and adult renal transplant recipients, potentially modifiable risk factors (obesity, hypertension, tobacco use, diabetes, abnormal lipids and lipoproteins, C-reactive protein and elevated serum homocysteine) associated with the development of CAD are quite common (23). Adult patients on dialysis are known to be at a far higher risk for development of CAD than kidney transplant recipients (24). However, adult renal transplant recipients remain at a higher risk for the development of CAD than the general population (24). It is likely that the increased risk for CAD in transplant recipients is due, in part, to the effects of immunosuppression or other factors related to the transplant (25,26). It is also possible, however, that some of the increased risk for CAD is due to the aspects of renal failure not completely corrected by a kidney transplant.

At this time, little is known of long-term outcomes (3,4) or the prevalence of CAD in children and young adults following pediatric renal transplantation. Data from the North American Pediatric Renal Transplant Cooperative Study relate cardiopulmonary factors as cause of death in 15.6% of children who had received a transplant, but in only 7.4% of those with a functioning graft (27). The United States Renal Data System Annual Data Report reports cardiac death as the cause of death in 22.6% of all patients who died with functioning grafts under the age of 30 (28). These reports, however, are from registry data and it is difficult to determine if the cardiac deaths were due to atherosclerotic CAD

as opposed to cardiac arrest, cardiomyopathy, arrhythmias or other causes of cardiac dysfunction such as pericarditis or valvular heart disease.

Little data exist regarding the presence of CAC in adult or pediatric renal transplant patients. Oh et al. found that the duration of ESRD and cumulative time undergoing dialysis were significantly associated with CAC in a population of 39 young adults 19–39 years of age treated with dialysis (n = 13) and transplantation (n = 26). CAC was detectable in 92% of patients, with higher CAC scores present among those on dialysis compared to those who were transplanted. Symptoms of cardiovascular disease were reported in 20% of their patients, but it is not possible to tell from the data presented if these were transplant patients or patients on dialysis. In addition, it is not possible to determine if these patients had undergone transplantation as children, although it appears that most were transplanted after the age of 18. It is implied, but not explicitly stated, that most if not all patients had received dialysis prior to undergoing transplantation. In contrast, in the current study the vast majority of our patients received preemptive transplants (79%) without being exposed to dialysis. The higher prevalence of CAC found in their study compared to ours may be due to the widespread exposure to dialysis and the longer mean time on dialysis in their transplant patients compared to our patients (mean peritoneal dialysis 18 months and hemodialysis 28 months compared to 6.6 months for our seven patients who received dialysis and 2.4 months for all 19 patients) (13).

In support of this hypothesis, Goodman et al. performed EBCT studies on 39 young adults on hemodialysis and peritoneal dialysis and found substantial amounts of CAC in patients as young as 20 years (12). In their study, a high percentage of dialysis patients (87%) between 20 and 30 years of age developed severe CAC at an even younger age than our group of transplant recipients. The amount of CAC was strongly associated with length of time on dialysis. A similar study in older dialysis patients confirmed these findings and found even more CAC in older chronic dialysis patients (29). Thus, the findings by Goodman et al. are consistent with differences between our study and that by Oh et al.

The main drawbacks of EBCT scanning to identify those at high- risk for CAD relate to its high- cost and its somewhat low specificity as a screening tool. Methods to measure CAC should become more commonly available as cardiac-gated multidetector computed tomography provides another widely available technology to quantify CAC (30,31) The overall usefulness of EBCT and multidetector computed tomography, compared to other noninvasive modalities to assess subclinical CAD, and the significance of CAC in asymptomatic adults from the general population is currently being studied through the ongoing multicenter 10-year Multi-Ethnic Study of Atherosclerosis (MESA) sponsored by the NIH (32).

Our pilot study is a step toward determining long-term cardiac risks and outcomes after pediatric renal transplantation. The mean CAC scores of patients from our study group who had detectable CAC (mean age 39 years) were comparable to a median age- and sex-matched male population aged 55–80 years and a female population aged 75–80 years (16–18). Our patients had multiple clinical and laboratory-based risk factors associated with the development of CAD. Thus, they are likely to remain at further increased risk for the development of coronary atherosclerosis and CAD compared to the general population.

Recent guidelines from the National Kidney Foundation suggest that adolescents with kidney transplants should be considered in the highest risk category for coronary heart disease for risk factor management. Under these guidelines, adolescents would be evaluated for dyslipidemia at presentation, after change in kidney status, and then annually. Treatment by therapeutic life-style change (diet) would be followed by treatment with a lipid-reduction agent if no improvement was seen (33). Close attention to hypertension, obesity and glucose control were also suggested.

In conclusion, our pilot study suggests that young adults who received kidney transplants as children are at increased risk for the early development of CAC, which has been strongly linked to the presence of coronary atherosclerosis and CAD. Larger cohort studies are needed to confirm and extend our findings and should include tracking the progression of CAC in transplant patients and determining whether risk factor reduction can decrease the risk of CAD associated cardiac morbidity and mortality.

Acknowledgments

The comparison data was provided by grant R01 HL46292 from the National Institutes of Health and a General Clinic Research Center grant from the National Institutes of Health (M-01 RR00585) awarded to Mayo Clinic Rochester. This paper was presented in part at the American Transplant Congress 2003, Washington, D.C., May 31, 2003–June 4, 2003.

References

1. UNOS website, www.optn.org
2. North American Pediatric Renal Transplant Cooperative Study, 2004. 5–3, website: http://spitfire.emmes.com/study/ped/resources/annlrept2004.pdf
3. McDonald SP, Craig JC. Australian and New Zealand Paediatric Nephrology Association. Long-term survival of children with end-stage renal disease. N Engl J Med 2004; 350: 2654–2662.
4. Milliner DS. Pediatric renal-replacement therapy—coming of age. N Engl J Med 2004; 350: 2637–2639.
5. Kasiske BL, Guijarro C, Massy ZA, Weiderkehr MR, Ma JZ. Cardiovascular disease after renal transplantation. J Am Soc Nephrol 1990; 7: 158–165.
6. Rumburger JA, Simons B, Fitzpatrick L, Sheedy PF, Schwartz RS. Coronary artery calcium area by electron beam computed tomography and coronary artery atherosclerotic plaque area.

A histopathologic correlative study. Circulation 1995; 92: 2157–2162.
7. Kaufmann RB, Sheedy PF 2nd, Maher JE et al. Quantity of coronary artery calcium detected by electron beam computed tomography in asymptomatic subjects and angiographically studied patients. Mayo Clin Proc 1995; 70: 223–232.
8. Bielak LF, Rumberger JA, Sheedy PF 2nd, Schwartz RS, Peyser PA. Probabilistic model for prediction of angiographically defined obstructive coronary artery disease using electron beam computed tomography calcium score strata. Circulation 2000; 102: 380–385.
9. Rumberger JA, Brundage BH, Rader DJ, Kondos G. Electron beam computed tomographic coronary calcium scanning: a review and guidelines on use in asymptomatic persons. Mayo Clin Proc 1999; 74: 243–252.
10. Raggi P, Callister TQ, Cooil B et al. Identification of patients at increased risk of development of first unheralded acute myocardial infarction by electron beam computed tomography. Circulation 2000; 101: 850–855.
11. Arad Y, Spadaro LA, Goodman K, Newstein D, Guerci AD. Prediction of coronary events with electron beam computed tomography. J Am Coll Cardiol 2000; 36: 1253–1260.
12. Goodman WG, Goldin J, Kuizon B et al. Coronary-artery calcification in young adults with end-stage renal disease who are undergoing dialysis. N Engl J Med 2000; 342: 1478–1483.
13. Oh J, Wunsch R, Turzer M et al. Advanced coronary and carotid arteriopathy in young adults with childhood-onset chronic renal failure. Circulation 2002; 106: 100–105.
14. Reed JE, Rumberger JA, Davitt PJ, Kaufmann RB, Sheedy PF 2nd. System for quantitative analysis of coronary artery calcification via electron beam computed tomography. In: *Medical imaging, 1994: Physiology and Function from Multidimensional images*. Proc SPIE 1994; 2168: 43–53.
15. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr., Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardial 1990; 15: 827–832.
16. Royston P. A parametric model for ordinal response data, with application to estimating age-specific reference intervals. Biostatistics 2001; 1: 263–277.
17. Lange LA, Lange EM, Bielak LF et al. Autosomal genome-wide scan for coronary artery calcification loci in sibships at high risk for hypertension. Arterioscler Thromb Vasc Biol 2002; 22: 418–423.
18. Bielak LF, Peyser PA, Sheedy PF 2nd. Electron beam computed tomography screening for asymptomatic coronary artery disease. Semin Roentgenol 2003; 38: 39–53.
19. Grundy SM. Age as a risk factor: you are as old as your arteries [editorial]. AJC 1999; 83: 1455–1457.
20. Sangiorgi G, Rumberger JA, Severson A et al. Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden in humans; A histologic study of 723 coronary artery segments using non-decalcifying methodology: electron beam computed tomography and coronary artery disease: scanning for coronary artery calcification. J Am Coll Cardiol 1998; 31: 126–133.
21. Schmermund A, Denktas AE, Rumberger JA et al. Independent and incremental value of coronary artery calcium for predicting the extent of angiographic coronary artery disease: comparison with cardiac risk factors and radionuclide perfusion imaging. J Am Coll Cardiol 1999; 34: 777–786.
22. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. JAMA 2004; 291 210–215.
23. Eknoyan G and Levin NW. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: evaluation classification, and stratification. Am J Kidney Dis 2002; 39: S1–S266.
24. Wolfe RA, Ashby VB, Milford EL et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. N Engl J Med 1999; 341: 1725–1730.
25. Ovuworie CA, Fox ER, Chow CM et al. Vascular endothelial function in cyclosporine and tacrolimus treated renal transplant recipients. Transplantation 2001; 72 : 1385–1388.
26. Kramer BK, Zulke C, Kammerl MC et al. Cardiovascular risk factors and estimated risk for CAD in a randomized trial comparing calcineurin inhibitors in renal transplantation. Am J Transplant 2003; 3: 982–987.
27. North American Pediatric Renal Transplant Cooperative Study. 2004. 7–3, website: http://spitfire.emmes.com/study/ped/resources/annlrept2004.pdf.
28. Parekh RS, Carroll CE, Wolfe RA, Port FK. Cardiovascular mortality in children and young adults with end-stage kidney disease. J Pediatr 2002; 141: 191–197.
29. Braun J, Oldendorf M, Moshage W, Heidler R, Zeitler E, Luft FC. Electron beam computed tomography in the evaluation of cardiac calcifications in chronic dialysis patients. Am J Kidney 1996; 27: 394–401.
30. Maher JE, Bielak LF, Raz JA, Sheedy PF 2nd, Schwartz RS, Peyser PA. Progression of coronary artery calcification: a pilot study. Mayo Clin Proc 1999; 74: 347–55.
31. Carr JJ, Nelson JC, Wong ND et al. Calcified coronary artery plaque measurement with cardiac CT in population-based studies: standardized protocol of Multi-Ethnic Study of Atherosclerosis (MESA) and Coronary Artery Risk Development in Young Adults (CARDIA) study. Radiology 2005; 234: 35–43.
32. NIH website: www.nih.gov/news/pr/sep2000/nhlbi-14.htm
33. Kasiske B, Cosio FG, Beto J et al. National Kidney Foundation. Clinical practice guidelines for managing dyslipidemias in kidney transplant patients: a report from the Managing Dyslipidemias in Chronic Kidney Disease Work Group of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative. Am J Transplant 2004; 4: 13–53.