Transpl Int (1996) 9: 221–226


ORIGINAL ARTICLE

**David C. Wheeler**
**Ruth Morgan**
**David M. Thomas**
**Mary Seed**
**Alan Rees**
**Richard H. Moore**

# Factors influencing plasma lipid profiles including lipoprotein (a) concentrations in renal transplant recipients

Received: 16 June 1995
Received after revision: 4 December 1995
Accepted: 7 December 1995

D.C. Wheeler[1] (✉) · D.M. Thomas · R.H. Moore
Renal Transplant Unit,
Cardiff Royal Infirmary,
Cardiff, CF2 1SZ, Wales, UK

R. Morgan · A. Rees
Department of Medicine,
University of Wales College of Medicine,
Cardiff, CF4 4XN, Wales, UK

M. Seed
Department of Medicine,
Charing Cross and
Westminster Medical School,
London, W6 8RF, UK

[1]*Present address:*
Department of Nephrology,
University Hospital Birmingham
NHS Trust,
The Queen Elizabeth Hospital,
Edgbaston, Birmingham B15 2TH, UK
Fax: + 44 121 627 2527

**Abstract** Fasting plasma cholesterol, triglycerides, high-density lipoprotein (HDL) and apoprotein (apo) B were elevated in 214 non-diabetic renal transplant recipients when compared to a reference group. Apo (a) was slightly but not significantly lower in transplant recipients (median 118 mg/dl, range 16–1680 vs 130 mg/dl, 10–1176) and this difference could be predicted from Lp (a) isoform analysis. Cholesterol, triglyceride, apo B and apo (a) concentrations correlated negatively with creatinine clearance but none of these parameters showed a significant association with proteinuria. Patients treated with steroids had higher plasma HDL concentrations than those receiving cyclosporin monotherapy ($P < 0.01$). The use of diuretics was associated with raised triglycerides ($P < 0.001$) and cholesterol ($P < 0.01$) and with reduced HDL ($P < 0.01$) whilst patients receiving β-blockers had significantly higher triglycerides ($P < 0.01$) and lower HDL levels ($P < 0.02$). In multiple regression analysis, age ($P < 0.01$), creatinine clearance ($P < 0.05$) and diuretic therapy ($P < 0.005$) were independent risk factors for increased cholesterol whilst apo (a) levels correlated negatively with creatinine clearance ($P < 0.005$). These results suggest that impaired renal function, steroids and non-immunosuppressive drugs contribute to lipid abnormalites in renal transplant recipients.

**Key words** Lipoprotein (a), kidney transplantation · Apoprotein (a), kidney transplantation · Cholesterol, kidney transplantation · Kidney transplantation, cholesterol · Kidney transplantation, hyperlipidaemia

## Introduction

With advances in immunosuppressive therapy and in the treatment of infection, cardiovascular disease has emerged as a leading cause of death in long-term survivors of renal transplantation and occurs more frequently than in the general population [21, 38]. Hyperlipidaemia is common in such patients and represents a potentially correctable risk factor [22, 24]. The profile of lipid abnormalities observed following renal transplantation has been well characterised although fewer studies have examined Lp(a) concentrations. In addition, despite our knowledge of the characteristic lipid profiles observed in these patients, the pathogenesis of abnormal lipid metabolism following renal transplantation is not clearly understood [29].

Studies in non-renal patients have defined certain patterns of lipid and lipoprotein abnormality that are associated with increased cardiovascular risk including high levels of total and low-density lipoprotein (LDL) cholesterol and reduced HDL concentrations [9, 25, 36]. In addition, elevated levels of Lp(a) have been recognised as an independent risk factor for cardiovascular disease [3, 31]. This lipoprotein is similar to LDL but

contains an additional glycoprotein, apo (a), which is structurally similar to plasminogen [34]. Plasma concentrations of Lp(a) are strongly influenced by a gene on the long arm of chromosome 6 that determines the isoforms secreted by the liver, high molecular weight isoforms being associated with low plasma levels and vice versa [7]. Elevated Lp(a) levels have been noted in patients with chronic renal failure on renal replacement therapy and have been associated with the development of cardiovascular disease in this population [11, 35]. In addition, some recent reports have documented elevated levels of this lipoprotein in renal transplant recipients [8, 17, 44].

Based on studies in the general population, it seems likely that correction of lipid abnormalities may reduce the risk of cardiovascular disease following renal transplantation [28]. A better understanding of the factors that contribute to abnormal lipid metabolism in this group of patients may help in the planning of rational treatment strategies. In addition, investigation of Lp (a) concentrations in patients with renal disease may improve our understanding of the metabolism of this lipoprotein. The aim of this study was to examine factors influencing plasma lipid and lipoprotein profiles in a large group of renal transplant recipients, with particular reference to Lp(a).

## Materials and methods

### Subjects

Two hundred and fourteen renal transplant recipients attending follow-up were recruited for this study over a 6-month period. All patients had received their grafts at least 12 months prior to the start of this period and had stable renal function. Diabetic subjects, patients receiving lipid-lowering drugs and those in whom immunosuppressive therapy had been modified within the previous 3 months in response to biopsy-proven acute rejection were excluded. The reference group was recruited from patients who were being investigated for chest pain. Coronary angiography demonstrated that these patients had essentially clear coronary arteries. More detailed demographic data on this group of individuals has already been published, the age and sex distribution being essentially similar to that of the transplant patient population [27]. No patients in this reference group had biochemical evidence of renal disease. Mean (SD) plasma triglyceride was 1.9 (1.0) mmol/l and cholesterol 5.9 (1.3) mmol/l.

### Lipid, lipoprotein and apolipoprotein measurements

A single 10-ml sample of blood was venesected from each patient following an overnight fast and after a 24-h period of urine collection. Serum was separated by centrifugation, aliquoted into smaller volumes and stored at –20 °C. Total cholesterol and triglycerides were assayed using standard enzymatic procedures [1, 42]. HDL cholesterol was measured after phosphotungstate/magnesium precipitation [43] and LDL cholesterol was calculated using the Friedewald formula [14]. Apolipoproteins A1, B and (a) were quantified using an immunoradiometric assay (Kabi Pharmacia Diagnostics). The apo (a) assay utilised two different monoclonal antibodies in excess and measured apo (a) levels after prior reduction/hydrolysis of the apo (a) peptide from the Lp(a) particle. All samples were assayed in duplicate. Lipoprotein (a) phenotyping was performed by horizontal SDS polyacrylamide gel electrophoresis followed by electroblotting and immunostaining. The separated apo (a) isoforms were then detected by treating the membrane with sheep polyclonal anti-apo(a) antibodies followed by rabbit anti-sheep antibodies conjugated with horseradish peroxidase. The migration rates of isoforms were measured relative to a fast migrating band [44].

**Table 1** Patient demographics

| | |
|---|---|
| Age (years) | 44.7 ± 14.2 |
| Sex (number) | 89 male, 125 female |
| Weight (kg) | 70.6 ± 15.2 |
| Smokers | 24 % |
| Ex-smokers | 23 % |
| Glucose (mmol/l) | 5.65 ± 0.98 |
| Creatinine (μmol/l) | 180 ± 95 |
| Creatinine clearance (ml/min) | 44 ± 19.9 |
| Proteinuria (g/l) | 0.89 ± 2.01 |
| Immunosuppressive regimen | |
| Cyclosporin | 25 % |
| Cylosporin/Prednisolone | 15 % |
| Cyclosporin/Prednisolone/Azathioprine | 24 % |
| Cyclosporin/Azathioprine | 6 % |
| Prednisolone/Azathioprine | 28 % |
| Azathioprine | 0.5 % |
| Prednisolone | 1.5 % |
| Antihypertensive therapy | |
| β-blocker | 47 % |
| Diuretic | 52 % |
| Calcium antagonist | 43 % |
| ACE inhibitor | 12 % |

### Statistical analysis

All analyses were performed using the Statistical Package for the Social Sciences. Variables conforming to a Gaussian distribution were compared using Student's *t*-test whilst those that did not [triglycerides and apo (a)] were either analysed using a Mann-Whitney U-test or logarithmically transformed prior to comparison with Student's *t*-test. Significance tests on discrete groups were performed using the chi-square test. Lp(a) isoforms were assessed by fixed bin analysis [32]. Multiple regression analysis was conducted using cholesterol and apo (a) as the dependent variables.

## Results

The clinical and demographic details of the study group are shown in Table 1 and the lipid profiles in Table 2. The transplant group was characterised by elevated levels of cholesterol, triglycerides, LDL, HDL and Apo B and lower levels of Apo A1 than the reference group. Although apo (a) levels were lower in the renal transplant group than in the reference population, this differ-

**Table 2** Differences in plasma lipid profiles between transplant patients and reference group. All values represent means ± SD except triglycerides and Apo (a), which are expressed as median (range).

| | Transplant ($n = 214$) | Reference ($n = 109$) | $P$ value |
|---|---|---|---|
| Cholesterol (mmol/l) | 7.2 ± 1.6 | 5.9 ± 1.3 | < 0.01 |
| LDL (mmol/l) | 4.9 ± 1.4 | 4.2 ± 1.1 | < 0.01 |
| Triglycerides (mmol/l) | 1.9 (0.5–8.3) | 1.6 (0.6–5.6) | < 0.01 |
| HDL (mmol/l) | 1.2 ± 0.3 | 0.9 ± 0.3 | < 0.01 |
| Apo A1 (mg/dl) | 134 ± 39 | 150 ± 41 | < 0.01 |
| Apo B (mg/dl) | 139 ± 40 | 85 ± 28 | < 0.01 |
| Apo (a) (U/l) | 118 (16–1680) | 130 (10–1176) | NS |

**Table 3** Lipoprotein (a) phenotypes in transplant and reference populations. Subjects possessing isoforms B, S1 or S2 were compared with those possessing isoforms S3, S4 or the null type using fixed bin analysis. Using a chi-square test there was a significant difference in phenotype between the two groups ($P < 0.0001$).

| Phenotype | Transplant group | Reference group |
|---|---|---|
| B/X<br>S1/X<br>S2/X | 24<br>(12 %) | 39<br>(40 %) |
| S3/X<br>S3/X<br>S3/S4<br>Null | 170<br>(88 %) | 59<br>(60 %) |

ence was not statistically significant. Lp(a) isoform distribution in the two groups was consistent with this finding (Table 3), with the transplant group having an increased frequency of high molecular weight isoforms (S3 and S4) that are associated with lower apo (a) levels.

The effects of drug therapy on lipid and lipoprotein levels are shown in Table 4. The use of ACE inhibitors and calcium antagonists did not appear to influence plasma lipid levels significantly. Patients treated with either β-blockers (atenolol) or diuretics (furosemide) had higher plasma triglyceride and lower HDL levels than those not receiving these drugs. Diuretic therapy was also associated with increased cholesterol, LDL and apo B concentrations. Of the various immunosuppressive regimens used (Table 1), the only significant association found was a higher mean HDL (and apo A1) concentration in patients receiving prednisolone. Neither antihypertensive nor immunosuppressive drugs appeared to influence plasma Lp(a) concentrations.

The relationship between graft function and lipid profile is shown in Table 5. There were significant negative correlations between lipid and lipoprotein levels and creatinine clearance. The correlation between apo (a) and proteinuria did not reach statistical significance ($P = 0.059$), but there was a positive correlation between apo (a) and cholesterol ($r = 0.1912$, $P = 0.003$).

The variables that influenced cholesterol levels were determined by multiple regression analysis (Table 6). When the demographic, drug and renal functional parameters were included in the equation, four variables – creatinine clearance, diuretic therapy, age and sex – were found to be significant determinants of cholesterol concentrations. A similar analysis using apo (a) as the dependent variable did not identify any explanatory variables, although creatinine clearance was of borderline significance (data not shown).

## Discussion

The major lipid and lipoprotein abnormalities observed in the renal transplant patients were higher plasma concentrations of cholesterol, triglycerides, HDL and LDL than in the reference group. Levels of the LDL apoprotein, apo B, were also elevated, as were the calculated levels of LDL cholesterol, suggesting increased plasma levels of this lipoprotein particle. These results are largely consistent with the pattern of dyslipidaemia now widely reported in renal transplant recipients except

**Table 4** Effect of therapy on plasma lipid levels in renal transplant recipients. No significant associations were found between plasma lipid or apoprotein levels and the use of calcium antagonists, angiotensin-converting enzyme inhibitors, cyclosporin or azathioprine (*NS* not significant)

| Drug therapy | | Cholesterol (mmol/l) | LDL (mmol/l) | Log trigs (mmol/l) | HDL (mmol/l) | Apo A1 (mg/dl) | Apo B (mg/dl) | Apo (a)[a] (U/l) |
|---|---|---|---|---|---|---|---|---|
| β-blockers | Yes | 7.3 ± 1.6 | 5.0 ± 1.4 | 0.33 ± 0.19 | 1.17 ± 0.34 | 139 ± 42 | 142 ± 39 | 103 |
| | No | 7.1 ± 1.7 | 4.9 ± 1.5 | 0.24 ± 0.22 | 1.29 ± 0.33 | 133 ± 34 | 135 ± 40 | 109 |
| | *P* value | NS | NS | < 0.01 | < 0.02 | NS | NS | NS |
| Diuretics | Yes | 7.5 ± 1.7 | 5.2 ± 1.5 | 0.34 ± 0.19 | 1.16 ± 0.32 | 131 ± 37 | 147 ± 41 | 104 |
| | No | 6.8 ± 1.6 | 4.7 ± 1.4 | 0.24 ± 0.21 | 1.29 ± 0.35 | 137 ± 40 | 130 ± 36 | 108 |
| | *P* value | < 0.01 | < 0.01 | < 0.001 | < 0.01 | NS | < 0.01 | NS |
| Prednisolone | Yes | 7.3 ± 1.6 | 5.0 ± 1.4 | 0.28 ± 0.20 | 1.28 ± 0.36 | 138 ± 39 | 140 ± 40 | 104 |
| | No | 6.9 ± 1.7 | 4.7 ± 1.5 | 0.30 ± 0.22 | 1.12 ± 0.26 | 124 ± 36 | 134 ± 39 | 110 |
| | *P* value | NS | NS | NS | < 0.01 | < 0.05 | NS | NS |

[a] Expressed as Mann-Whitney mean rank

**Table 5** Relationship between graft function and lipid profile

| | Correlations with creatinine clearance: | |
|---|---|---|
| | Coefficient ($r$) | $P$ value |
| Cholesterol | −0.1791 | 0.005 |
| LDL | −0.1614 | 0.011 |
| Triglycerides | −0.1856 | 0.004 |
| HDL | 0.0532 | NS |
| Apo A1 | −0.1534 | 0.014 |
| Apo B | −0.2229 | 0.001 |
| Apo (a) | −0.1775 | 0.005 |

**Table 6** Factors influencing plasma cholesterol as assessed by multiple regression analysis

| Dependent variable | Explanatory variables | $P$ value |
|---|---|---|
| Cholesterol | Age | 0.005 |
| | Sex | 0.03 |
| | Creatinine clearance | 0.02 |
| | Diuretic therapy | 0.004 |

that HDL cholesterol concentrations are usually reported to be normal in this population [22, 24, 29]. The HDL cholesterol levels in our transplant population are similar to those reported by other investigators in comparable study populations, thus raising the possibility that this lipoprotein, which is thought to protect against cardiovascular disease, was abnormally low in the reference population [8, 44]. In addition, since levels of the major HDL apoprotein, apo A1, were lower in the transplant patients than in the reference group, the significance of this finding has to be questioned. Although plasma levels of HDL are reduced in patients with chronic renal failure, we did not find a correlation between plasma HDL and creatinine clearance in our transplant patients [33].

Certain antihypertensive medications were associated with plasma lipid abnormalities, and the use of such agents would appear to be an important factor in the pathogenesis of post-transplant hyperlipidaemia. Patients receiving either furosemide or atenolol had higher plasma triglyceride and lower HDL cholesterol levels than the remainder of the group, whilst the use of diuretics was also associated with higher plasma cholesterol concentrations. In contrast, calcium antagonists did not appear to influence plasma lipid levels. The contribution of β-blockers and diuretics to post transplant dyslipidaemia has been noted by other investigators and these observations emphasise the importance of considering adverse effects on lipid profiles when prescribing antihypertensive drugs to renal transplant recipients [5, 10, 19, 23]. Calcium antagonists, α-blockers and angiotensin converting enzyme inhibitors have little effect on plasma lipids and may be a more suitable choice in this respect [2, 30].

The use of immunosuppressive therapy has been implicated in the pathogenesis of post transplant hyperlipidaemia. For example, steroid dose has been correlated with plasma triglyceride levels in several studies [5, 10, 22, 23]. We were unable to demonstrate such a relationship although the use of prednisolone in any combination of immunosuppressive regimen was associated with higher HDL concentrations. The role of cyclosporin in the pathogenesis of post-transplant lipid abnormalities has been controversial. Although altered lipid metabolism has been attributed to cyclosporin therapy by a number of investigators [4, 16] and improvements in lipid profiles reported after withdrawing this immunosuppressive agent [16], a more recent study has shown no correlation between plasma levels of cyclosporin and lipids [41]. In our study there was no association between cyclosporin usage and lipid abnormalities.

Since hyperlipidaemia is a recognised complication of chronic renal failure, the possible impact of declining graft function on the pathogenesis of lipid abnormalities was examined. Decreased creatinine clearance was associated with elevated triglyceride, cholesterol and apo B levels and was an independent risk factor for hypercholesterolaemia in multiple regression analysis. Creatinine clearance also correlated inversely with plasma Lp(a) concentrations. Whilst these relationships could be causal, hypercholesterolaemia has recently been implicated as an aetiological factor in the pathogenesis of chronic graft rejection, and the association between raised plasma lipid concentrations and allograft injury warrants further investigation [13]. Hyperlipidaemia may also contribute to the progression of chronic renal failure in native kidneys [26], and it has been suggested that individuals possessing apo (a) isoforms associated with higher Lp(a) levels may be more susceptible to kidney disease in the clinical setting of diabetes [20]. Our data demonstrating that such isoforms were under-represented in a population of patients with end-stage renal failure who had received kidney transplants would not support this hypothesis.

Since an association between proteinuria and hyperlipidaemia is well recognised and has been demonstrated in renal transplant recipients [5, 22, 23], we examined the possible impact of urinary protein excretion on plasma lipid levels in our study population. Only 10 % of patients had urinary protein losses greater than or equal to 3.0 g/l and no significant correlation was found with any of the lipid parameters studied.

A number of recent studies have documented elevated levels of Lp(a) in patients with chronic renal failure [11, 12, 15, 35, 39]. This abnormality appears to be present prior to institution of dialysis treatment [15] and cannot be accounted for by genetic factors [12]. Lp(a) is also elevated in proteinuric patients with moderately impaired renal function but does not correlate with creatinine clearance in this group, suggesting that

different mechanisms are involved [37, 40]. Lp(a) is synthesised in the liver and both uraemia and proteinuria may lead to an increase in hepatic production [34]. Indeed, increased hepatic lipoprotein synthesis is one mechanism by which urinary protein loss may lead to elevated plasma lipid levels in the nephrotic syndrome [46]. Alternatively, the kidney may play a role in Lp(a) catabolism, although at present there is no experimental evidence to support this possibility. Studies examining Lp(a) levels in renal transplant recipients have produced conflicting results, with both normal [6, 18] and elevated [8, 17, 44] levels reported. Cyclosporin therapy was identified as one possible factor contributing to an increase in Lp(a) concentrations [45]. We found slightly lower levels of this lipoprotein in our transplant population than in the reference group, a difference that could be entirely accounted for by the difference in distribution of Lp(a) phenotypes between the two groups. Furthermore, we found no association between Lp(a) concentrations and the use of cyclosporin. This would suggest that Lp(a) levels are not influenced by renal transplantation. We did note a positive association between Lp(a) and cholesterol levels, and whilst there was a tendency for plasma concentrations of this lipoprotein to correlate with urinary protein excretion, this association did not reach conventional statistical significance, possibly because of the small number of patients involved. In a multiple regression analysis, creatinine clearance was of borderline significance in determining plasma Lp(a) levels, a finding that supports earlier studies demonstrating elevated plasma levels of this lipoprotein in uraemia [11, 12, 15, 35, 39].

The discrepancy between Lp(a) levels reported in this and other studies could be due to a number of different factors. Since more than 90% of the variability of plasma Lp(a) is genetically determined, it is possible that the presence of different alleles on the apo(a) locus may account for some of the variation between study populations. Four studies did not include Lp(a) isoform data, raising the possibility that differences between reference and study groups were biased by genetic factors [6, 8, 17, 18]. However, despite noting elevated Lp(a) levels, Webb et al. reported similar distributions of Lp (a) isoforms [44]. Other factors that might influence Lp(a) levels, such as graft function and urinary protein excretion, might differ between our own and the other study populations.

In conclusion, our results identify non-immunosuppressive drugs, particularly diuretics, and impaired renal function as important factors associated with hyperlipidaemia complicating renal transplantation. In contrast to several previous studies, we demonstrated normal plasma levels of Lp(a) in renal transplant recipients. Since Lp(a) is elevated in uraemic individuals, renal transplantation may have a beneficial effect in terms of correcting cardiovascular risk factors in patients with chronic renal failure. When treating hypertension in such individuals, it may be prudent to choose drugs that do not exacerbate plasma lipid abnormalities.

## References


1. Allain CC, Poon LS, Chan CSG, Richmond W, Fu PC (1974) Enzymatic determination of total serum cholesterol. Clin Chem 20: 470–475
2. Ames RP (1986) The effect of antihypertensive drugs on serum lipids and lipoproteins. II. Non-diuretic drugs. Drugs 32: 335–357
3. Armstrong VW, Cremer P, Eberle E, Manke A, Schulze F, Wieland H, Kreuzer H, Seidel D (1986) The association between serum Lp(a) concentrations and angiographically assessed coronary atherosclerosis. Atherosclerosis 62: 249–257
4. Ballantyne CM, Podet EJ, Patsch WP, Harati Y, Appel V, Gotto AM, Young JB (1989) Effects of cyclosporine therapy on plasma lipoprotein levels. JAMA 262: 53–56
5. Bittar AE, Ratcliffe PJ, Richardson AJ, Raine AEG, Jones L, Yudkin PL, Carter R, Mann JI, Morris PJ (1990) The prevalence of hyperlipidaemia in renal transplant recipients. Transplantation 50: 987–992
6. Black IW, Wilcken DEL (1992) Decreases in apoliprotein (a) after renal transplantation: implications for lipoprotien (a) metabolism. Clin Chem 38: 353–357
7. Boerwinkle E, Menzel HJ, Kraft HG, Utermann G (1989) Contribution of Lp(a) glycoprotein phenotypes to normal lipid variation. Hum Genet 82: 73–78
8. Brown JH, Anwar N, Short CD, Bhatnager D, Mackness MI, Hunt LP, Durrington PN (1993) Serum lipoprotein (a) in renal transplant recipients receiving cyclosporin monotherapy. Nephrol Dial Transplant 8: 863–867
9. Castelli WP, Garrison RJ, Wilson PWF, Abbott RD, Kalousdian S, Kannel WB (1986) Incidence of coronary heart disease and lipoprotein cholesterol levels. The Framingham Study. JAMA 256: 2835–2838
10. Chan MK, Varghese Z, Persaud JW, Fernando ON, Moorhead JF (1981) The role of multiple pharmaco-therapy in the pathogenesis of hyperlipidaemia after renal transplantation. Clin Nephrol 15: 309–313
11. Cressman MD, Heyka RJ, Paganini EP, O'Neill J, Skibinski CI, Hoff HF (1992) Lipoprotein (a) is an independent risk factor for cardiovascular disease in haemodialysis patients. Circulation 86: 475–482
12. Dieplinger H, Lackner C, Kronenberg F, Sandholzer C, Lhotta K, Hoppichler F, Graf H, König P (1993) Elevated plasma concentrations of lipoprotein (a) in patients with end-stage renal disease are not related to the size polymorphism of apolipoprotein (a). J Clin Invest 91: 397–401
13. Dimény E, Fellström B, Larsson E, Tufveson G, Lithell H (1993) Chronic vascular rejection and hyperlipoproteinemia in renal transplant patients. Clin Transplant 7: 482–490

14. Friedewald WT, Levy RI, Fredickson DS (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 18: 499–502
15. Haffner SM, Gruber KK, Aldrete G, Morales PA, Stern MP, Tuttle KR (1992) Increased lipoprotein (a) concentrations in chronic renal failure. J Am Soc Nephrol 3: 1156–1162
16. Harris KPG, Russell GI, Parvin SD, Veitch PS, Walls J (1986) Alterations in lipid and carbohydrate metabolism attributable to cyclosporin A in renal transplant recipients. BMJ 292: 16
17. Heimann P, Josephson MA, Fellner SK, Thistlethwaite JR, Stuart FP, Dasgupta A (1991) Elevated lipoprotein (a) levels in renal transplantation and haemodialysis patients. Am J Nephrol 11: 470–474
18. Irish AB, Simons LA, Savdie E, Hayes JM, Simons J (1992) Lipoprotein (a) levels in chronic renal disease states, dialysis and transplantation. Aust N Z J Med 22: 243–248
19. Jackson JM, Lee HA (1982) The role of propranolol therapy and proteinuria in the aetiology of post renal transplantation hyperlipidaemia. Clin Nephrol 18: 95–100
20. Kapelrud H, Bangstad H-J, Dahl-Jørgensen K, Berg K, Hanssen KF (1991) Serum Lp(a) lipoprotein concentrations in insulin dependent diabetic patients with microalbuminuria. BMJ 303: 675–678
21. Kasiske BL (1988) Risk factors for accelerated atherosclerosis in renal transplant recipients. Am J Med 84: 985–992
22. Kasiske BL, Umen AJ (1987) Persistent hyperlipidaemia in renal transplant patients. Medicine (Baltimore) 66: 309–316
23. Lowry RP, Soltys G, Mangel R, Kwiterovitch P, Sniderman AD (1987) Type II hyperlipoproteinaemia, hyperapobetalipoproteinaemia, and hyperalphaliproteinaemia following renal transplantation: prevalence and precipitating factors. Transplant Proc 19: 2229–2232
24. Markell MS, Friedman EA (1989) Hyperlipidaemia after organ transplantation. Am J Med 87 [Suppl 5N]: 61N–67N
25. Martin MJ, Hulley SB, Browner WS, Kuller LH, Wentworth D (1986) Serum cholesterol blood pressure and mortality: implications from a cohort of 361,622 men. Lancet II: 933–936
26. Moorhead JF, Wheeler DC, Varghese Z (1989) Glomerular structures and lipids in progressive renal disease. Am J Med 87 [Suppl 5N]: 12–20N
27. Morgan R, Bishop AJ, Young WT, Ephraim DC, Matthews SB, Rees A (1992) The relationship between apolipoprotein (a), lipid and lipoprotein levels and the risk of coronary artery disease. Cardiovasc Risk Factors 2: 105–111
28. Muldoon MF, Manuck SB, Matthews KA (1990) Lowering cholesterol concentrations and mortality: a quantitative review of primary prevention trials. BMJ 301: 309–314
29. Pirsch JD, D'Alessandro AM, Sollinger HW, Knechtle SJ, Reed A, Kalayoglu M, Belzer FO (1992) Hyperlipidaemia and transplantation: etiologic factors and therapy. J Am Soc Nephrol 2: S238–S242
30. Pollare T, Lithel H, Berne C (1989) A comparison of the effects of hydrochlorothiazide and captopril on glucose and lipid metabolism in patients with hypertension. N Engl J Med 321: 868–873
31. Rosengren A, Wilhelmsen L, Eriksson E, Risberg B, Wedel H (1990) Lipoprotein (a) and coronary heart disease: a prospective case-control study in a general population sample of middle aged men. BMJ 301: 1248–1251
32. Sandholzer C, Saha N, Kark JD, Rees A, Jaross W, Dieplinger H, Hoppichler F, Boerwinkle E, Utermann G (1992) Apo(a) isoforms predict risk for coronary heart disease. A study in six populations. Arterioscler Thromb 12: 1214–1226
33. Savdie E, Gibson JC, Stewart JH, Simons LA (1979) High-density lipoprotein in chronic renal failure and after renal transplantation. BMJ 1: 928–930
34. Scanu AM, Fless GM (1990) Lipoprotein (a): heterogeneity and biological relevance. J Clin Invest 85: 1709–1715
35. Shoji T, Nishizawa Y, Nishitani H, Yamakawa M, Morii H (1992) High serum lipoprotein (a) concentrations in uraemic patients treated with continuous ambulatory peritoneal dialysis. Clin Nephrol 38: 271–276
36. Simons LA (1986) Interrelations of lipids and lipoproteins with coronary artery disease mortality in 19 countries. Am J Cardiol 57: 5–10G
37. Stenvinkel P, Berglund L, Heimbürger O, Pettersson E, Alvestrand A (1993) Lipoprotein (a) in nephrotic syndrome. Kidney Int 44: 1116–1123
38. The US Renal Data system (1990) Excerpts from United States Renal Data System 1990 annual report: VI. Survival and mortality. Am J Kidney Dis 16: 44–52
39. Thillet J, Faucher C, Issad B, Allouache M, Chapman J, Jacobs C (1993) Lipoprotein (a) in patients treated by continuous ambulatory peritoneal dialysis. Am J Kidney Dis 22: 226–232
40. Thomas ME, Freestone A, Varghese Z, Persaud JW, Moorhead JF (1992) Lipoprotein (a) in patients with proteinuria. Nephrol Dial Transplant 7: 597–601
41. Vathsala A, Weinberg RB, Schoenberg L, Grevel J, Dunn J, Goldstein RA, Van Buren CT, Lewis RM, Kahan BD (1989) Lipid abnormalities in renal transplant recipients treated with cyclosporin. Transplant Proc 21: 3670–3673
42. Wahlefeld AW (1974) Triglycerides. Determination after enzymatic hydrolysis. In: Bergmeyer HU (ed) Methods of enzymatic analysis. 2nd English edn. Verlag Chemie, Weinheim/Academic Press, New York, pp 1831–1835
43. Warnick GR, Nguyen T, Albers AA (1985) Comparison of improved precipitation methods for quantification of high density lipoprotein cholesterol. Clin Chem 31: 217–222
44. Webb AT, Plant M, Reaveley DA, O'Donnell M, Luck VA, O'Connor B, Seed M, Brown EA (1992) Lipid and lipoprotein (a) concentrations in renal transplant patients. Nephrol Dial Transplant 7: 636–641
45. Webb AT, Reaveley DA, O'Donnell M, O'Connor B, Seed M, Brown EA (1993) Does cyclosporin increase lipoprotein (a) concentrations in renal transplant recipients? Lancet 341: 268–270
46. Wheeler DC, Bernard DB (1994) Lipid abnormalities in the nephrotic syndrome: causes, consequences and treatment. Am J Kidney Dis 23: 331–346