Dear Sir,

We have read with interest the original paper by Hong et al. [1] about the relationship between lipoprotein(a) levels and fibrinolytic activity in patients with nephrotic syndrome and we would like to add our experience on this subject.

We prospectively measured serum concentrations of lipids, apoproteins Al, B, CII, CIII, lipoprotein(a), fibrinogen, renal function, proteinuria fibrinopeptide A (FPA), beta-thromboglobulin (BTG) and platelet factor 4 (PF4) in a sample of 30 patients with biopsy-proven active nephrotic syndrome. There were 20 males and 10 females, age 45 ± 16, BMI 23.6 ± 1.7, serum creatinine 2.1 ± 1.4 mg/dl, fibrinogen 6.8 ± 2.4 g/l, proteinuria 6.5 ± 2 g/day, total cholesterol: 410 ± 250 mg/dl, HDL C 45 ± 11 mg/dl, LDL C 296 ± 112 mg/dl, triglycerides 295 ± 110 mg/dl, serum albumin 2.5 ± 1 g/l, apo Al 125 ± 15 mg/dl, apo B 180 ± 10 mg/dl, apo CII 14 ± 6 mg/dl, apo CIII 24 ± 7 mg/dl, Lp(a) median 35 mg/dl, interquartile range [10-80]. The etiology of nephrotic syndrome was as follows: minimal change disease (n = 5), focal glomerulosclerosis (n=10), membranous nephropathy (n = 6), IgA glomerulonephritis (n = 9). The reference values were obtained from a matched group of 30 healthy volunteers. Patients were prospectively followed for a period of 48 months in order to analyze the evolution of serum lipoprotein levels and Lp(a) levels and to investigate the occurrence of thrombotic episodes. Every 6 months, we determined serum lipid and Lp(a) levels, 24-hour proteinuria and we also performed a Doppler study of the femoral veins, renal veins, cava and suprahepatic veins. All patients with minimal change disease and 5 patients with focal glomerulosclerosis were treated with steroids. Four patients with membranous nephropathy were treated with steroids plus cyclophosphamide. All nonresponding patients were treated with enalapril (5-20 mg/day). During the nephrotic phase, patients showed levels of cholesterol (410 ± 250 vs. 198 ± 42, p < 0.001), LDL C (296 ± 112 vs. 128 ± 16, p < 0.001), apo CII (14 ± 6 vs. 4.5 ± 2, p < 0.001), apo CIII (24 ± 7 vs. 6 ± 2.5, p < 0.001), and Lp(a) (35 [10-80] vs. 14 [1-56], p < 0.001), significantly higher than those of the healthy controls. Likewise, the levels of FPA (2.5 ± 1 ng/ml vs. 1 ± 0.65, p < 0.001) and BTG (45 ± 18 vs. 23 ± 10 ng/ml, p < 0.001) were higher in nephrotic patients than those of the healthy controls. The serum level of PF4 was not different from that of controls (6 ± 4 ng/ml vs. 5 ± 2.5
ng/ml). Lp(a) levels correlated positively with total cholesterol (r 0.7, p < 0.01), LDL C (r 0.75, p < 0.01), apo B (r 0.58, p < 0.05), serum fibrinogen (r 0.66, p < 0.05), serum creatinine (r 0.45, p < 0.05) and urinary protein excretion (r 0.6, p < 0.01) and correlated negatively with serum albumin (r 0.5, p < 0.01). In spite of the positive correlation between Lp(a) and proteinuria, 6 patients (12%) showed Lp(a) levels in the normal range. Nine treated patients (5 with minimal change disease, 2 with focal glomerulosclerosis and 2 with membranous nephropathy) achieved complete remission. In these patients, both serum lipids and Lp(a) normalized. During follow-up, 3 out of the 21 (14.7%) patients with persistent nephrotic syndrome suffered a thrombotic episode (1 femoral deep thrombosis, 1 asymptomatic unilateral vein thrombosis (confirmed by phlebogram) and 1 renal vein thrombosis with pulmonary embolism. These 3 patients showed serum albumin levels lower (1.9 ± 0.2 vs. 2.9 ± 0.4, p < 0.05) and serum fibrinogen levels higher (8.5 ± 1.5 vs. 4.0 ± 0.7 g/l, p < 0.01) than patients without thrombosis, but only one of them showed significantly elevated Lp(a) levels (15 mg/dl, NS, 17 mg/dl, NS, and 24 mg/dl, p < 0.05, respectively). The FPA, BTG and FP4 levels of these patients were not different from those of patients without thrombosis. After introducing enalapril treatment, no significant changes could be observed either in serum lipids, Lp(a) levels or in 24-hour urine protein excretion. Follow-up of Lp(a) demonstrated that in proteinuric patients, the serum Lp(a) levels suffered little variation with time. Since the prothrombotic effect of Lp(a) has been attributed to a competitive inhibition of plasminogen activation, one would expect to find high Lp(a) levels in patients suffering from thrombotic complications. The 3 patients who suffered thrombotic episodes had a severe nephrotic syndrome with marked proteinuria and increased cholesterol levels. However, since the Lp(a) levels in our patients were not always significantly elevated, we argue that other factors exist which could well account for these thrombotic events. We wish to point out that although Lp(a) levels are significantly elevated in patients with nephrotic syndrome [1-3] and data provided by a number of authors suggest that Lp(a) may decrease the fibrinolytic activity both in nephrotic [1] and nonnephrotic patients [4], the clinical relevance of this fact is unclear and some patients may suffer thrombotic episodes with Lp(a) levels in the normal range.

References

Lipoprotein(a) Levels and Fibrinolytic Activity in Patients with Nephrotic Syndrome
Nephron 1996;73:102-103