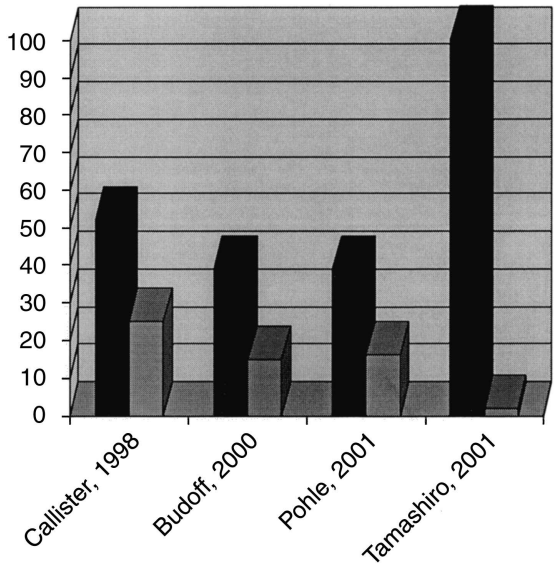

Fig. 1. Progression of calcium score as measured by electron beam tomography in coronaric artery in people with different lipid status. Faster progression was associated with high lipids in all studies (at least 10 months of follow-up). Callister (*N Engl J Med* 339:1972, 1998, cited by Chertow, Burke, and Raggi) reported a 52% rate of progression in patients with coronary artery disease left untreated versus 25% in patients treated with 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors and low-density lipoprotein (LDL) cholesterol. Budoff (*Am J Cardiol* 86:8, 2000) reported 39% versus 15% in the presence of statin therapy in asymptomatic subjects. Pohle *(Circulation* 104:1927, 2001) reported 39% in patients with aortic valve calcification versus 16% in those with low LDL. Tamashiro et al (*Am J Kidney Dis* 38:64–69, 2001) reported a faster rate of progression in dialysis patients with high trygliceride and low high-density lipoprotein (HDL) cholesterol (the absolute number, $+432 \pm 458$ versus $+7.5 \pm 31$ are changed in percentage in this figure to obtain an homogeneous picture)

vascular calcification is an active process, did hypercalcemic patients also lack any progression?

Finally, since calcium and sevelamer patients should have different acid-base status, was there a relationship between serum bicarbonate and calcification progression? Evidence shows that, to prevent vasculopathy, it is important to avoid hypercalcemia (not normal calcemia) by perhaps lowering the acceptable high end calcium range in order to reduce the risk of unwanted escape in addition to hyperphosphoremia, dyslipemia, alkalosis, and other medial manifestations.

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REFERENCES

1. Chertow GM, Burke SK, Raggi P, for the Treat to Goal Working Group: Sevelamer attenuates the progression of coronary and aortic calcification in hemodialysis patients. *Kidney Int* 62:245–252, 2002
2. Braun J, Oldendorf M, Moshage W, *et al*: Electron beam computed tomography in the evaluation of cardiac calcification in chronic dialysis patients. *Am J Kidney Dis* 27:394–401, 1996
3. Tamashiro M, Iseki K, Sunagawa O, *et al*: Significant association between the progression of coronary artery calcification and dyslipidemia in patients on chronic hemodialysis. *Am J Kidney Dis* 38:64–69, 2001
4. Arad Y, Spadaro LA, Roth M, *et al*: Serum concentration of calcium, 1,25 vitamin D and parathyroid hormone are not correlated with coronary calcifications. An electron beam computed tomography study. *Coronary Artery Dis* 9:513–518, 1998

To the Editor: Although the study by Chertow et al has shown that in hemodialysis patients, sevelamer compared to calcium-based phosphate binders is less likely to cause hypercalcemia and arterial calcifications, we do not think that in the patients of this study sevelamer should replace $CaCO_3$. Indeed, their mild hyperparathyroidism could have been corrected by just higher doses of $CaCO_3$ alone without aluminum hydroxide [$Al(OH)_3$] or calcitriol. In fact, a high dose of $CaCO_3$, without the co-administration of calcitrol, offers the distinct advantage of maintaining lower serum-phosphate concentration without higher serum calcium [1]. This is probably due to the fact that calcitriol increases intestinal absorption of phosphate whereas $CaCO_3$ decreases it.

Therefore, to clinically justify the preferential use of "sevelamer plus calcitriol" over that of $CaCO_3$, the lower risk of arterial calcification should have been demonstrated against higher doses of $CaCO_3$ without calcitriol while actually obtaining in both groups the same "targeted" ranges for serum concentrations of parathyroid hormone, calcium, and phosphate. The issue is indeed to know whether despite comparable serum chemistry, the higher oral doses of calcium are actually increasing the arterial calcium load more than calcitriol. However, the negative direct bone mineralization effect of calcitriol shown in vitamin D-receptor knockout mice [2] does not support this possibility.

The second issue is to know whether prevention of arterial calcification will improve cardiovascular risk independently of the improvement of uremic dyslipidemia, which promotes atherosclerosis and therefore intimal calcification. Indeed, the control of dyslipidemia with statin decreases cardiovascular morbid mortality in high-risk patients [3] and is much cheaper than sevelamer as a cholesterol-lowering drug.

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REFERENCES

1. Indridason OS, Quarles LD: Comparison of treatments for mild secondary hyperparathyroidism in hemodialysis patients. Durham Renal Osteodystrophy Study Group. *Kidney Int* 57:282–292, 2000
2. Kinuta K, Tanaka H, Shinohara M, Kato S, *et al*: Vitamin D is a negative regulating factor in bone mineralization. *J Bone Miner Res* 15(Suppl 1):S180, 2000
3. Heart Protection Study Collaborative group: MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: A randomised placebo-controlled trial. *Lancet* 360:7–22, 2002

To the Editor: In their unblinded study of vascular calcification in dialysis patients, Chertow et al combine results from patients receiving calcium acetate with those from patients receiving calcium carbonate. Use of these calcium salts interchangeably in studies is not appropriate since calcium acetate is a more potent phosphate binder with less calcium absorption [1]. This can be seen in the study of Chertow et al by the differences in required doses. If the hypothesis concerning the relationship of calcification to oral calcium advanced by the authors is correct, it would be very useful to see the study results analyzed for each salt separately in order to test for dose response effects. This is particularly important because the average daily dose of calcium acetate required by patients in this study was nearly equivalent to the USRDA for calcium.

It is likely that the sevelamer patients received supplemental calcium (as shown by the absence of change in serum calcium levels over the course of the year and that some also experienced hypercalcemia). Traditionally, in studies of sevelamer, 1 gram of supplemental calcium is often given to prevent hypocalcemia [2]. This dose is nearly equivalent to the calcium dose utilized by Chertow et al in the calcium treatment arm. Clearly, there was also opportunity for adjustment of the calcium content of dialysis baths and vitamin D. If the sevelamer patients did indeed receive additional calcium from supplements and dialysis solutions, conclusions concerning the culpability of oral calcium in vascular calcification are not valid.

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REFERENCES

1. Mai ML, Emmett M, Sheikh MS, *et al*: Calcium acetate, an effective phosphorus binder in patients with renal failure. *Kidney Int* 36:690–695, 1989
2. Bleyer AJ, Burke SK, Dillon M, *et al*: A comparison of the calcium-free phosphate binder sevelamer hydrochloride with calcium acetate in the treatment of hyperphosphatemia in hemodialysis patients. *Am J Kidney Dis* 33:694–701, 1999

To the Editor: In the July 2002 issue of *Kidney International*, Chertow et al reported that treatment with sevelamer or calcium-based phosphate binders results in equivalent serum phosphorus control (mean, 5.1 mg/dL). This finding is surprising since mean phosphorus levels achieved with sevelamer in previous studies were consistently above 6.0 mg/dL [1]. Moreover, we believe that the study design is critically flawed since it failed to control for other variables potentially important in the progression of cardiovascular calcification, including the type of calcium-containing binder (calcium acetate is twice as effective as calcium carbonate yet contains half the amount of elemental calcium), dialysate calcium, vitamin D dose, and lipid levels. Did sevelamer-treated patients receive a nighttime calcium supplement or increased dialysate calcium to prevent hypocalcemia? Were there differences in progression of calcification between calcium acetate- and calcium carbonate-treated patients? Since vitamin D increases calcium absorption and hypercalcemia risk, and may itself predispose to cardiovascular calcification [2], Chertow et al should have controlled for vitamin D use. In the calcium-treated patients, low-density lipoprotein (LDL) cholesterol should have been controlled to an equivalent level with 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors. Given failure to adequately control other important variables, this study by Chertow et al clearly does not establish a causal relationship between cardiovascular calcification and possible calcium loading from calcium-containing binders. We, therefore, believe that this study by Chertow et al does not justify preferential use of the considerably more expensive phosphate binder sevelamer hydrochloride. Finally, could the metabolic acidosis in this and other studies be explained by an acid load provided by sevelamer hydrochloride [3].

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REFERENCES

1. Chertow GM, Burke SK, Dillon MA, *et al*: Long-term effects of sevelamer hydrochloride on the calcium x phosphate product and lipid profile of haemodialysis patients. *Nephrol Dial Transplant* 14:2907–2914, 1999
2. Milliner DS, Zinsmeister AR, Lieberman E, Landing B: Soft tissue calcification in pediatric patients with end-stage renal disease. *Kidney Int* 38:931–936, 1990
3. Gallieni M, Cossoline M, Brancaccio D: Transient decrease of serum bicoarbonate levels with sevelamer hydorchoride as the phosphage binder. *Kidney Int* 52:1776–1777, 2000

Reply from the authors

We are grateful to the authors of these letters for their interest in our work and to the Editor for the opportunity