



# Myopathy and Less Frequent Complications of Cystinosis

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**A**lthough not initially recognized when there were few long-term survivors with cystinosis, the use of renal transplantation in the 1960s permitted observation of a number of additional clinical disabilities, as patients with nephropathic cystinosis survived past young childhood for the first time. Among these, serious distal myopathy has emerged as a significant problem of early adulthood in untreated or poorly cysteamine-compliant patients. Untreated or poorly compliant patients with cystinosis exhibit cystine crystals in muscles and highly elevated muscle cystine content. This vacuolar myopathy is characterized by electromyographic abnormalities, type I muscle fiber atrophy, and begins distally and proceeds centrally. The myopathy is progressive and in some cases impairs patient mobility. In 1993, one-third of 36 adult patients with cystinosis seen at the National Institutes of Health displayed distal myopathy, and 21 of 31 had swallowing difficulty. Only 11 of the 36 had been adequately treated with cysteamine, however, 5 of 11 patients treated with cysteamine also developed myopathy, compared with 7 of 25 untreated patients who developed this complication.<sup>1</sup> This study was conducted while cysteamine was still an investigational drug; hence, many of the patients designated as treated may not have been on cysteamine until early adolescence. A more recent study found 5 of 11 patients with cystinosis older than 18 years and treated with cysteamine had myopathy.<sup>2</sup>

## Other Less Frequent Extra-Renal Complications

### Cardiac and Vascular Complications

Heart involvement does not typically occur in younger patients with cystinosis but has been described in a few patients. One had recurrent restrictive cardiomyopathy in early childhood attributed to uremia and insufficient dialysis. He then had recurrence in his teens and twenties and died of a ruptured pseudoaneurysm, restrictive cardiomyopathy, and congestive heart failure at age 33 years. Extensive cystine crystals and elevated cardiac cystine were found at autopsy.<sup>3</sup> Vascular calcifications have been described in chronic kidney disease and in 13 of 41 postrenal transplant patients with cystinosis who underwent computed tomography scans. The majority, 11 of 13, displayed coronary artery calcifications, and 2 had calcification of the vertebral arteries, or the thoracic great vessels. The calcifications were not attributable to hypertension, elevated lipid levels above the patients not showing calcifications, or abnormalities in serum calcium and phosphorus concentrations. The calcifications did correlate with older age, and time not on cysteamine (**Figure**).<sup>4</sup> Patients with cystinosis display hyperlipidemia and may be treated with statins and diet therapy.<sup>5</sup>

### Gastrointestinal Complications

Gastrointestinal concerns are not a frequent problem as a result of the primary disease process. Hepatomegaly and some pathologic abnormalities are seen in cystinosis, occasionally accompanied by nodular hyperplasia, but not cirrhosis.<sup>5</sup> Cysteamine therapy is the primary cause of gastrointestinal complaints. The agent is a free thiol, and consequently has the taste and odor of rotten eggs. This leads to nausea, vomiting, anorexia, and occasionally diarrhea in many patients, which often subsides with time, but in some may result in serious compliance issues. The side effect may be treated with a proton pump inhibitor to suppress the gastric hyperacidity, which is known to result from cysteamine administration.<sup>5,6</sup> ■

## Author Disclosures

The author declares no conflicts of interest, real or perceived.

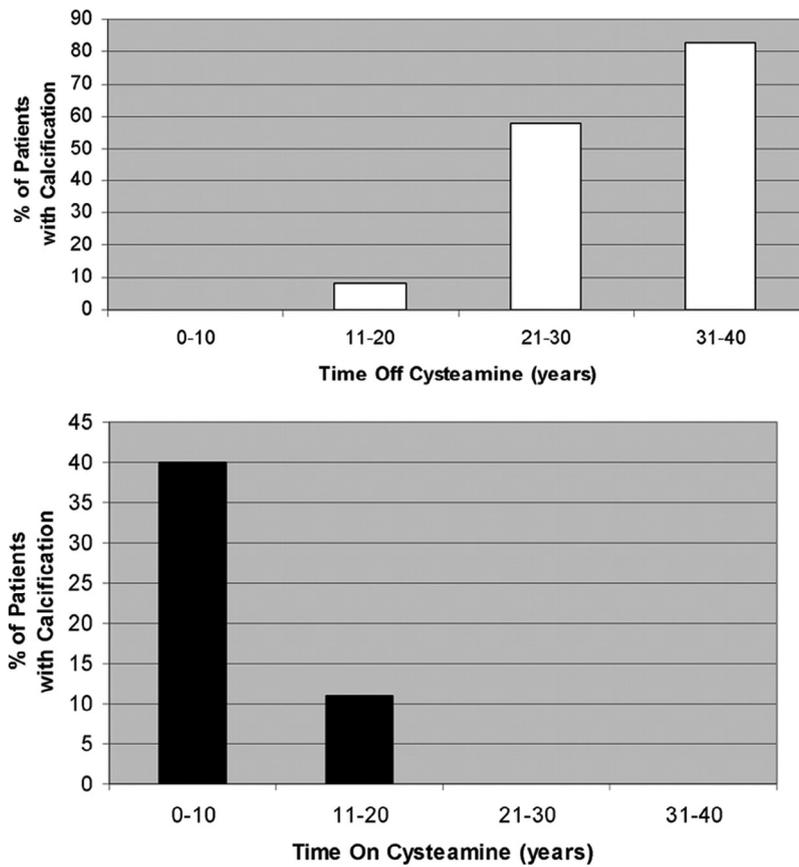
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**Figure.** Percent of cystinosis patients with vascular calcifications according to time off and on cysteamine therapy. Reprinted with permission from Ueda et al.<sup>4</sup>

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