Prevalence of Pompe disease in 3,076 patients with hyperCKemia and limb-girdle muscular weakness.

We prospectively screened a large European cohort of patients presenting with hyperCKemia and/or limb-girdle muscular weakness (LGMW) for acid ß-glucosidase (GAA) deficiency by dried blood spot (DBS) investigation. DBS were collected from 3,076 consecutive adult patients from 7 German and British neuromuscular centers. All specimens were investigated for GAA deficiency by fluorometry. Samples with reduced enzyme activity were subsequently investigated for GAA gene mutations. Of 3,076 patients with DBS samples, 232 patients (7.6%) showed low GAA enzyme activity. Of these 232 patients, 55 (24%) presented with isolated hyperCKemia and 176 (76%) with hyperCKemia and LGMW. With both features present, 94% of the patients showed a low enzymatic activity. Mutational analysis found GAA gene mutations in 74 patients (2.4%); herein 70 patients were heterozygote for the common GAA gene splice-site mutation c.-32-13T>G. The most common clinical presentation in the confirmed Pompe cohort was a limb-girdle phenotype (85.3%) combined with ventilatory insufficiency (61%).
Isolated hyperCKemia was found in 12%, while 2.7 had hyperCKemia and ventilatory insufficiency only. In a large cohort of unselected adult patients with hyperCKemia and/or LGMW, we found a prevalence of late-onset Pompe disease of 2.4%. Therefore, targeted screening of such a population should be encouraged in clinical practice.