Glycogen storage disease type IV (GSD IV) is an ultra-rare, autosomal recessive disorder caused by pathogenic variants in GBE1. Reduced or deficient glycogen branching enzyme activity occurs, and glycogen accumulation is impaired. This condition is typically characterized by abnormal polysaccharide accumulation and aggregates in liver tissues. GSD IV is a clinically heterogeneous disorder with presentations in utero, infancy, early childhood, or in middle to late adulthood (the latter referred to as Adult Polyglucosan Body Disease, or APBD). This guideline is the first consensus on diagnosing and managing patients with GSD IV, including APBD.

ABSTRACT
Glycogen storage disease type IV (GSD IV) is an ultra-rare, autosomal recessive disorder caused by pathogenic variants in GBE1. Reduced or deficient glycogen branching enzyme activity occurs, and glycogen accumulation is impaired. This condition is typically characterized by abnormal polysaccharide accumulation and aggregates in liver tissues. GSD IV is a clinically heterogeneous disorder with presentations in utero, infancy, early childhood, or in middle to late adulthood (the latter referred to as Adult Polyglucosan Body Disease, or APBD). This guideline is the first consensus on diagnosing and managing patients with GSD IV, including APBD.

BACKGROUND
Glycogen serves as a storage form of glucose in humans. Glycogen synthesis takes place in all tissues throughout the body, predominantly in the liver and skeletal muscle. It is stored as large, branched polymers of glucose residues and is involved in many physiological processes. The first enzyme that initiates glycogen synthesis is glycogen synthase (GYS). This enzyme catalyzes the formation of alpha-1,4-linked glycosyl units into an alpha-1,6 position, thus creating branched glycogen. Glycogen serves as a storage form of glucose in humans. Glycogen synthesis takes place in all tissues throughout the body, predominantly in the liver and skeletal muscle. It is stored as large, branched polymers of glucose residues and is involved in many physiological processes.

RESULTS
This guideline provides practical steps to confirm a GSD IV diagnosis and best practices for medical management, including:
- Imaging of the liver, heart, skeletal muscle, brain, and spine
- Functional and neuromusculoskeletal assessments
- Laboratory investigations
- Liver and heart function tests
- Long-term follow-up care

GSD IV, including APBD, is a multisystem disorder with variable primary tissue manifestations, including hepatic, muscular, neurologic, and/or cardiac involvement. Patients present with a wide range of difficult-to-manage symptoms and are best cared for by a multidisciplinary team led by a physician with expertise in this disorder. Team members should include a metabolic disease specialist, a medical geneticist, and other specialists dictated by the disease manifestations.

CONCLUSIONS
GSD IV, including APBD, is a complex, multisystem disorder with variable primary tissue manifestations. Patients present with a wide range of difficult-to-manage symptoms and therefore require comprehensive, multidisciplinary evaluations to assess and treat hepatic, muscular, neurologic, and/or cardiac involvement. Additionally, longitudinal, multidisciplinary follow-up is essential for all patients, regardless of age, at initial presentation or symptoms. The psychological and emotional impact of this disease on the patients, their families, and their caregivers should also be considered.

REFERENCES

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APBD = Adult-onset Peripheral neuropathy. Bladder dysfunction Decreased energy