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Hepatic and muscular glycogen storage diseases: A narrative review of therapeutic interventions and long-term outcomes

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Abstract:
Glycogen storage diseases (GSDs) are inherited metabolic disorders affecting hepatic or muscular glycogen metabolism. Hepatic and muscular GSDs diverge fundamentally in pathophysiology, driving distinct clinical priorities and outcome measures. Hepatic GSDs require sustained systemic metabolic control, primarily dietary management, to prevent hypoglycemia and long-term complications such as hepatic adenomas and nephropathy. Muscular GSDs are managed through functional adaptation, including structured exercise training and, in Pompe disease, enzyme replacement therapy, to improve exercise tolerance and motor function. Despite these tailored strategies, complications persist in both forms, underscoring the need for phenotype-driven management and standardized outcome measures across the GSD spectrum.

Keywords: Glycogen storage diseases (GSDs); hepatic glycogen storage disease; muscular glycogen storage disease; metabolic control; therapeutic outcomes

Background:
Glycogen is the principal carbohydrate storage polymer in humans, with hepatic and muscular glycogen serving distinct metabolic functions **[1]**. Disorders of glycogen synthesis or degradation result in glycogen storage diseases (GSDs), a heterogeneous group of inherited metabolic conditions classified by enzyme deficiency and tissue involvement **[2]**. Hepatic GSDs are characterized by impaired hepatic glucose release, leading to fasting hypoglycemia and long-term complications including hepatic adenomas and, in certain subtypes, renal complications such as nephropathy **[3]**. In contrast, muscular GSDs present with localized skeletal muscle energy deficits, manifesting as exercise intolerance and episodic rhabdomyolysis, while systemic glucose homeostasis remains largely preserved **[4]**. Despite sharing a common basis in disordered glycogen metabolism, the tissue-specific roles of glycogen in liver versus skeletal muscle result in fundamentally different therapeutic priorities. Hepatic GSDs require sustained metabolic control to prevent hypoglycemia and mitigate long-term complications **[5]**, whereas muscular GSDs benefit from functional rehabilitation and exercise-based interventions that improve muscle function and aerobic capacity **[6]**. Long-term follow-up studies show that conventional management strategies, while improving metabolic control, do not fully prevent persistent complications in hepatic GSDs such as hepatic adenomas and nephropathy **[7]** and do not fully arrest disease progression in muscular GSDs, particularly respiratory decline in late-onset Pompe disease **[8]**. Emerging gene-based therapies aim to address the underlying genetic defects across multiple GSD subtypes, offering potential for both systemic metabolic correction in hepatic disease and localized functional improvement in muscular disease **[9, 10]**. Therefore, it is of interest to review the therapeutic interventions and clinical outcomes in hepatic and muscular glycogen storage diseases.

Therapeutic approaches in hepatic glycogen storage diseases:
Current evidence indicates that hepatic glycogen storage diseases (GSDs) are characterized by impaired glucose homeostasis and require sustained metabolic control to prevent fasting hypoglycemia and associated metabolic complications. Dietary management remains the cornerstone of therapy, particularly in GSD Ia, where uncooked cornstarch therapy provides a continuous source of glucose and contributes substantially to metabolic stability **[12, 13]**. Recent reviews further emphasize that maintaining metabolic control is essential not only for preventing acute hypoglycemia but also for reducing the risk of secondary complications such as dyslipidemia and growth impairment **[4, 14]**. In addition to dietary therapy, management strategies include individualized nutritional interventions and regular metabolic monitoring. Clinical studies in GSD VI and IX suggest that these disorders generally exhibit milder phenotypes and can often be managed successfully through dietary and metabolic control measures **[21]**. Nevertheless, strict adherence to treatment protocols and lifelong monitoring remain necessary because metabolic abnormalities may persist despite clinical improvement. For patients with severe hepatic involvement, particularly those with advanced hepatic dysfunction in GSD IV, liver transplantation represents an important therapeutic option. Studies have showed that liver transplantation can effectively correct the hepatic metabolic defect and improve survival outcomes **[15, 16]**. However, transplantation does not completely eliminate the risk of extrahepatic manifestations, indicating that long-term follow-up remains essential even after successful surgical intervention.

Long-term outcomes in hepatic glycogen storage diseases:
Long-term studies show that although contemporary management strategies have significantly improved survival and metabolic control, many patients continue to experience chronic complications. Persistent hepatic adenomas, nephropathy and other metabolic abnormalities remain important clinical concerns in adulthood **[17]**. These findings indicate that dietary management alone does not fully prevent disease progression or long-term sequelae. Comprehensive reviews have therefore emphasized the importance of lifelong surveillance programs in patients with hepatic GSDs **[14]**. Regular monitoring of liver function, renal status, metabolic parameters and potential hepatic malignancy risk is recommended to facilitate early detection of complications and optimize long-term outcomes. Consequently, hepatic GSDs should be viewed as chronic systemic disorders requiring multidisciplinary management throughout life.

Therapeutic approaches in muscular glycogen storage diseases:

In contrast to hepatic GSDs, muscular GSDs are characterized primarily by localized impairments in skeletal muscle energy metabolism while systemic glucose homeostasis remains largely preserved. Therapeutic strategies therefore focus on improving functional performance and reducing exercise intolerance rather than correcting systemic metabolic abnormalities. Exercise-based interventions represent a central component of management. Clinical guidelines and systematic reviews support the use of structured aerobic exercise programs to improve oxidative capacity, enhance exercise tolerance and promote functional adaptation in affected individuals **[11, 18]**. The "second wind" phenomenon observed in McArdle disease (GSD V) further illustrates the capacity for metabolic adaptation during exercise and has been associated with improved aerobic fitness and functional performance **[20]**. Nutritional interventions also differ from those used in hepatic disease. Short-term carbohydrate supplementation before physical activity may improve muscle glucose availability and delay symptom onset in selected patients **[11]**. These strategies are intended to maximize muscle function and reduce the frequency of exercise-induced symptoms, including fatigue and rhabdomyolysis.

Long-term outcomes in muscular glycogen storage diseases:

Long-term outcomes in muscular GSDs are generally evaluated using measures of physical function, exercise tolerance, mobility and quality of life. Studies consistently show that exercise training can improve functional capacity and reduce symptom burden; however, disease progression may continue despite intervention **[18]**. Pompe disease (GSD II) represents a notable example in which disease-specific therapy is available. Enzyme replacement therapy (ERT) has demonstrated significant benefits in stabilizing or improving motor function and ambulation in affected individuals **[19]**. Nevertheless, long-term follow-up studies indicate that respiratory decline may continue in some patients despite ongoing treatment, suggesting that ERT slows but does not completely halt disease progression **[22]**. These findings highlight the need for continued therapeutic development and long-term monitoring in muscular GSDs.

Comparative analysis of hepatic and muscular glycogen storage diseases:

Current evidence highlights a fundamental divergence between hepatic and muscular glycogen storage diseases that directly influences therapeutic priorities and outcome assessment. Hepatic GSDs function primarily as systemic disorders of glucose regulation and therefore require interventions directed toward metabolic control, prevention of hypoglycemia and monitoring for chronic complications **[4, 14]**. In contrast, muscular GSDs are characterized by localized deficits in muscle energy utilization and are managed primarily through exercise-based rehabilitation, functional adaptation and targeted therapies such as enzyme replacement therapy **[11, 18 and 19]**. Differences are also evident in the outcome measures used to evaluate treatment success. Studies involving hepatic GSDs typically focus on biochemical control and complication rates, whereas studies involving muscular GSDs emphasize exercise capacity, motor performance, respiratory function and quality-of-life outcomes **[18]**. This heterogeneity complicates direct comparison across GSD subtypes and highlights the need for standardized outcome frameworks in future research. Overall, the evidence supports phenotype-driven management strategies tailored to tissue-specific pathophysiology. While current therapies have improved patient outcomes considerably, significant challenges remain, including persistent long-term complications in hepatic disease and incomplete prevention of disease progression in muscular forms. Continued advances in molecular and gene-based therapies may help address these limitations and improve long-term outcomes across the spectrum of glycogen storage diseases **[10]**.

Conclusion:

Hepatic and muscular glycogen storage diseases represent two fundamentally distinct therapeutic challenges with divergent long-term outcomes. Hepatic GSDs require sustained metabolic control to prevent hypoglycemia and chronic complications, whereas muscular GSDs are managed through exercise-based functional adaptation and targeted therapies. These findings support phenotype-driven management and highlight the need for standardized outcome measures to better evaluate current and emerging treatments.

References:

[1] Gümüş E & Özen H. *World J Gastroenterol*. 2023 **29**:3932 [PMID: 37476587].
[2] Soon GST & Torbenson M. *Int J Mol Sci*. 2023 **24**:6133 [PMID: 37047105].
[3] Massese M *et al. Orphanet J Rare Dis*. 2022 **17**:241 [PMID: 35725468].
[4] Wright TLF *et al. Curr Opin Pediatr*. 2022 **34** :496 [PMID: 35942643].
[5] Kor D *et al. Orphanet J Rare Dis*. 2025 **20**:336 [PMID: 40760487].
[6] Tarnopolsky MA. *Continuum (Minneap Minn)*. 2022 **28**:1752 [PMID: 36537979].
[7] Kruger E *et al. J Health Econ Outcomes Res*. 2025 **12**:13 [PMID: 39790363].
[8] Dalmia S *et al. Cochrane Database Syst Rev*. 2023 12:CD012993. [PMID: 38084761].
[9] Chou JY & Mansfield BC. *Front Mol Med*. 2023 **3**:1167091 [PMID: 39086673].
[10] Koeberl DD *et al. Journal of inherited metabolic disease*. 2024 **47**:93 [PMID: 37421310].
[11] Lucia A *et al. Neuromuscul Disord*. 2021 **31**:1296 [PMID: 34848128].
[12] Hsu RH *et al. Mol Genet Genomic Med*. 2023 **11**:e2221 [PMID: 37272773].
[13] Derks TGJ *et al. Nutrients*. 2021 **13**:3828 [PMID: 34836082].
[14] Hannah WB *et al. Nat Rev Dis Primers*. 2023 **9**:46 [PMID: 37679331].
[15] Beyzaei Z *et al. Clinical transplantation*. 2023 **37**:e14867 [PMID: 36433721].
[16] Koch RL *et al. JCI Insight*. 2024 **9**:e177722 [PMID: 38912588].

ISSN 0973-2063 (online) 0973-8894 (print)
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©Biomedical Informatics (2026)

[17] Szymańska E *et al. Diagnostics (Basel, Switzerland)*. 2020 **10**:297 [PMID: 32414085].
[18] Bordoli C *et al. Therapeutic advances in rare disease*. 2022 **3**:26330040221076497 [PMID: 37180413].
[19] van der Beek NAME *et al. Curr Opin Neurol*. 2025 **38**:538 [PMID: 40471681].
[20] Salazar-Martínez E *et al. Front Physiol*. 2021 **12**:744632 [PMID: 34721068].
[21] Uçar SK *et al. Eur J Clin Nutr.* 2025 **79**:723 [PMID: 40211049].
[22] Winkler M *et al. Neuromuscular Disorders*. 2022 **32**:195 [PMID: 35120758].

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