REHABILITATION, CANCER, AND CONGENITAL BLEEDING DISORDERS

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ABSTRACT

Background
Patients with congenital bleeding disorders require more frequent monitoring and careful management of treatments to avoid bleeding complications. In this context, an attempt is made to investigate the literature regarding rehabilitating patients with cancer and hemophilia.

Materials and Methods
We analyzed the existing literature on cancer, hemophilia, von Willebrand disease, other rare bleeding disorders and rehabilitation using databases: Google Scholar, Scopus, and PubMed, and finally, we analyzed 33 scientific articles.

Results
Managing cancer in patients with congenital bleeding disorders, such as hemophilia A, B, von Willebrand disease, and others, requires careful evaluation of bleeding risk and the effect of antitumor treatments on blood coagulation. Generally, patients with hemophilia and von Willebrand disease do not have an increased risk of developing cancer compared to the general population. However, some research suggests that people with hemophilia may have a slightly increased risk of developing certain types of tumors compared to the general population such as liver cancer and non-Hodgkin lymphoma, due to chronic inflammation and cell damage from bleeding episodes and treatment. However, if a patient with a congenital bleeding disorder develops cancer, the treatment must be managed to minimise the risk of bleeding. While a direct link between congenital bleeding disorders and cancer is contentious regarding the rehabilitation in patients with congenital blood disorders and cancer, the literature is lacking and without a solid basis on which to conclude.

Conclusions
It is important for patients with congenital bleeding disorders to be screened regularly and to coordinate with an expert team, including hematologists, oncologists, and other specialists, for optimal management of their health. Due to the insufficient evidence in the literature, it would be interesting to investigate rehabilitation approaches in patients with cancer and congenital bleeding disorders.

KEY WORDS

REHABILITATION, CANCER, HEMOPHILIA, VON WILLEBRAND, CONGENITAL BLEEDING DISORDERS.

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INTRODUCTION

Hemophilia and Von Willebrand Disease (VWD) are more frequent congenital bleeding disorders that require proper management. Hemophilia patients have an increased risk of certain cancers; regular monitoring is important. Cancer treatments can also increase bleeding risks and may require adjustments to therapy. Rehabilitation interventions, such as physiotherapy and physical therapy, can help manage joint bleeding and improve the quality of life in patients with hemophilic arthropathy. However, limited evidence exists regarding rehabilitation and walking ability in these patients. Proper management and rehabilitation can enhance outcomes for individuals with congenital bleeding disorders, but further research is needed, particularly in cancer.

MATERIALS AND METHODS

We analyzed the existing literature on cancer, hemophilia, von Willebrand disease and rehabilitation using databases: Google Scholar, Scopus, and PubMed, using the term: "malignancy" AND "cancer" AND "hemophilia" AND "Von Willebrand" to assess the relationship between congenital bleeding disorders and cancer. To assess the relationship between congenital bleeding disorders and cancer we add the term "rehabilitation". In total, we analyzed 33 scientific articles.

RESULTS AND DISCUSSION

Hemophilia is a rare genetic bleeding disorder caused by a deficiency in one of the clotting factors in the blood (Hemophilia A, which is caused by a deficiency of clotting factor VIII, and Hemophilia B, which is caused by a deficiency of clotting factor IX.)[1]. Patients with hemophilia (PWH) may be at an increased risk of developing certain types of cancer, such as liver cancer and non-Hodgkin lymphoma, due to chronic inflammation and cell damage from bleeding episodes and treatment[2,3]. The incidence of cancer in the population with hemophilia is not significantly different compared to the general population. However, some research suggests that people with hemophilia may have a slightly increased risk of developing certain types of tumors compared to the general population[2]. Some cancer treatments can also increase the risk of bleeding in patients with hemophilia. Regular monitoring and screening are recommended to manage the increased cancer risk, and adjustments to replacement therapy may be needed during cancer treatment. Despite the potential link between hemophilia and cancer, proper management can minimise the risks and improve patient outcomes. The risk of bleeding or thrombosis in cancer patients depends on the type of cancer and the anticancer therapy received[4]. Regular monitoring, screening, and appropriate management can help minimise these risks. Bleeding and thrombotic complications are common in critically ill cancer patients, and understanding the relationship between the coagulation system and cancer is essential. Von Willebrand Disease (VWD) is an inherited bleeding disorder caused by deficient or defective plasma Von Willebrand Factor (VWF)[5–8]. VWF is a large multimeric glycoprotein that plays a crucial role in hemostasis by mediating platelet function and stabilising blood coagulation[9]. Studies have suggested an association between elevated levels of VWF and an increased risk of cancer, indicating a potential role of VWF in promoting the growth and spread of tumors. However, the association between cancer and VWD is not well-established, as only a few cases have been reported in the literature[10,11]. Hemophilia frequently results in bleeding into the joints, which can cause degenerative arthritis, permanent joint damage, chronic pain, decreased mobility, and loss of muscle tone. These complications have been linked to a reduction in the quality of life of affected individuals[12].There is no rehabilitation evidence in the literature on patients with congenital bleeding disorders and cancer; however, there is much evidence regarding the rehabilitation process of patients with congenital bleeding disorders. Hemophilic arthropathy is a complication caused by recurrent bleeding episodes, mostly occurring in the ankles, knees, and elbows[13]; this can result in pain, immobility, joint instability[14], and reduced physical performance, leading to limitations in daily activities[15]. Early physiotherapy interventions effectively prevent and manage these complications[16], with benefits including pain management, joint health maintenance, and improved activity participation[17]. However, controversy still exists regarding the most effective methods for managing patients with hemophilia[18]. In 2022 Elshennawy et Al. published a systematic review of randomised controlled trials with a meta-analysis on the effectiveness of physical therapy modalities in patients with hemophilia[19] . This study aimed to provide clinical evidence of the effectiveness and safety of various physical therapy interventions in patients with hemophilia. Outcomes reviewed included body function and structure, activity limitations, and participation in hemophilic arthropathy. However, in 35 randomised clinical trials (RCTs), only nine studies that applied manual therapy for patients with hemophilic arthropathy were included in the meta-analysis[20–26]. Overall manual therapy, therapeutic exercises, and other therapies effectively improved patients' joint health status and quality of life (QoL) with hemophilic arthropathy without side effects such as bleeding[19]. Most physical therapy interventions effectively and safely manage patients with hemophilic arthropathy[21]. Physical therapy exercises were associated with better cardiometabolic risk factor profiles, reduced risk of developing functional limitations, increased bone mass, and increased joint stability to control exaggerated joint movements, thus reducing pain and disability. In addition, pain reduction could be achieved by using laser therapy in pediatric patients with hemophilic arthropathy. Early and continuous prophylaxis and rehabilitation are required to reduce the consequences of recurrent arthropathy[19].

Gualtierotti *et al*. highlights the importance of early diagnosis and comprehensive treatment of hemophilic arthropathy to prevent joint damage and chronic pain. It discusses the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and physical therapy as initial interventions. In cases where these approaches are insufficient, the authors discuss the use of intra-articular injections of corticosteroids or viscosupplementation to provide relief[27]. Furthermore, the article explores emerging treatments such as radiofrequency ablation, platelet-rich plasma (PRP) therapy, and regenerative medicine techniques like mesenchymal stem cell therapy. These innovative approaches show promise in managing pain and promoting joint health in individuals with hemophilic arthropathy. The authors emphasize the importance of a multidisciplinary approach involving hematologists, orthopedic specialists, and pain management experts to tailor treatment plans to the individual patient's needs. They also highlight the need for further research and clinical trials to evaluate the efficacy and safety of these emerging approaches. Ove-

rall, the article provides a comprehensive overview of current and emerging strategies for pain management in hemophilic arthropathy, offering insights into potential advancements in the field. In 2021, Otaka *et al*. published a systematic review of the effectiveness of a self-monitoring approach using fitness trackers to improve walking ability in rehabilitation settings by considering several conditions, including hemophilia[28] . The evidence reported is that of Goto *et al*. The RCT investigated the effect of self-monitoring and a home-based exercise program in 37 patients with hemophilia. The final value of the timed 10-m walk was favourable to the intervention group. However, the difference was not statistically significant, and the mean difference (0.1-s) was very small when considered clinically. Indeed, no significant difference in knee muscle strength was observed between the intervention and control groups[29].

CONCLUSIONS

Patients with congenital bleeding disorders who develop cancer face a combined risk. It is important for patients with congenital bleeding disorders to be screened regularly and to coordinate with an expert team, including haematologists, oncologists, and other specialists, for optimal management of their health. Due to the insufficient evidence in the literature, it would be interesting to investigate rehabilitation approaches in patients with cancer and congenital bleeding disorders. The effect of chemotherapy on haemophilia is known as the effect of exercise in patients with bleeding disorders. However, these aspects are not combined in the literature in patients presenting with cancer, receiving chemotherapy, and having bleeding disorders. This work may seem heterogeneous, but it faithfully reports what is in the literature today. There is a substantial gap that needs to be filled with the collaboration of clinicians and physical therapists in writing rehabilitation protocols for patients with cancer and bleeding disorders. This topic turns out to be rare because the clinician tends to think immediately about therapy for bleeding management and cancer treatment, leaving aspects such as quality of life and pain reduction on the back burner.

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