responded by their parents/caregivers), between 12- and 17.9-years (adolescents), and 18-years or older (adults). A total of 387 mPwH responded to the questionnaires. Their median (Interquartile Range; IQR) age was 49.0-years (26.0–62.0), 340 (87.8%) were adults, 29 (7.5%) had past or current inhibitors, 197 (50.9%) had ever been treated with any clotting product, and 12 (3.1%) were currently on prophylaxis. Approximately 74% reported they perceived their disease was not serious or not serious at all, and the different activity groups responded similarly. Recent bleed at any site was reported by 24/47 (51.1%) non-adults, related to the previous quarter, and 96/340 (28.2%) adults, related to the previous year. Joint impairment was reported for 180 joints (22 perceived as severe) by 50/387 (12.9%) mPwH. Age at first hemarthrosis was 10.0 years [5.0–16.0] among 97 (25%) mPwH. Lifetime hospitalization due to joint surgery was reported by 31/358 (8.7%) mPwH. The analyses of PROMIS29 and RAND-26 (quality of life), and HAL (functional abilities) indicated good quality of life and functional abilities. mPwH who participated in the HiN-6 Study reported good social functioning and a non-impactant disease in their lives, although bleeds, joint impairment, and need for joint surgeries still occur.

https://doi.org/10.1016/j.htct.2024.09.942

ERECTILE DYSFUNCTION IS RELATED TO QUALITY OF LIFE, BUT NOT TO RISK FACTORS FOR CARDIOVASCULAR DISEASES, AMONG ADULT MEN WITH HEMOPHILIA

RM Camelo [a], AV Rocha [b], E Remor [c], BP Duarte [d], MCB Moura [d], NCM Costa [d], IM Costa [d], AM Vanderlei [d], TMR Guimaraes [d]

[a] *Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil*
[b] *Hospital Manoel Gonçalves de Sousa Moreira, Itaúna, MG, Brazil*
[c] *Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil*
[d] *Fundação de Hematologia e Hemoterapia de Pernambuco (HEMOPE), Recife, PE, Brazil*

Erectile Dysfunction (ED) is a multifactorial disease related to psychosocial determinants and Cardiovascular Disease (CVD). Since Adults with Hemophilia (AwH) may have impaired psychosocial functioning due to the disease and have a high risk of developing CVD, we assumed ED might be prevalent among them. We evaluated perceived ED using a validated self-reported questionnaire in AwH participating in a cross-sectional study to describe CVD and CVD risk factors (HemoCardio Study). Male AwH aged ≥30-years attending a Northeastern Brazilian Hemophilia Treatment Center were invited. Demographic and clinical/therapeutic hemophilia data were collected from medical files. Clinical/therapeutic data about CVD and CVD risk factors were obtained by interview, physical examination, and laboratory tests. Perceived ED was evaluated by the International Index of Erectile Function-Erectile Function Domain (IIEF-6) instrument. Quality of life (QoL) was evaluated by HemoLatin-QoL and EQ-5D. Well-being was evaluated by the Hemophilia Well-Being Index (HWBI). For all questionnaires, higher scores meant better outcomes. A total of 84 AwH was included in the main study. Of the 52 AwH who responded to the IIEF-6, median age was 42.0-years (Interquartile Range [IQR] 36.0–51.8), 43 (83%) had hemophilia A, and 25 (48%) were severe. Median IIFE-6 was 29.0 (IQR 25.3–30.0) and 13 (25%) perceived ED. Perceived ED was associated with severe hemophilia ($p = 0.025$), lower HemoLatin-QoL total score ($p = 0.010$), and lower EQ-5D index ($p = 0.038$), but fairly associated with the use of anti-hypertensive ($p = 0.043$) and antidiabetic ($p = 0.049$). HWBI did not differ between AwH who perceived or did not ED. IIEF-6 had a positive correlation with the emotional functioning domain of the HemoLatin-QoL ($n = 47$, $\varrho = 0.313$, $p = 0.032$), but not with HemoLatin-QoL total score, EQ-5D index, or HWBI. We could not find associations between CVD or CVD risk factors and perceived ED among AwH. However, perceived ED correlated with QoL.

https://doi.org/10.1016/j.htct.2024.09.943

GENETIC AND NON-GENETIC DETERMINANTS OF SUCCESSFUL IMMUNE TOLERANCE INDUCTION IN PEOPLE WITH SEVERE HEMOPHILIA A

I Oomen [a,b], RM Camelo [c,d], M Carcao [e], G Castaman [f], JCJ Eikenboom [d], K Fischer [g], WG Frank Leebeek [h], D Lillicrap [i], ME Mancuso [j], D Matino [k], DMN Di Minno [l], AB Mohseny [d], J Oldenburg [m], SM Rezende [c], GE Rivard [n], N Rydz [o], S Schols [p], Voorberg Jan [a,b], FMRA Callado [q], LEM Carvalho [r], VKB Franco [s], CS Lorenzato [t], K Fijnvandraat [a,b], S Gouw [a,d], on behalf of the International GO-ITI study group

[a] *University of Amsterdam, Amsterdam, The Netherlands*
[b] *Sanquin Research and Landsteiner Laboratory, Amsterdam, The Netherlands*
[c] *Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil*
[d] *Leiden University Medical Center, Leiden, The Netherlands*
[e] *Hospital for Sick Children, Toronto, Canada*
[f] *Careggi University Hospital, Florence, Italy*
[g] *University Medical Center Utrecht, Utrecht, The Netherlands*
[h] *Erasmus Medical Center, Rotterdam, The Netherlands*
[i] *Queen's University, Kingston, Canada*
[j] *IRCCS Humanitas Research Hospital, Milan, Italy*
[k] *McMaster University, Hamilton, Canada*
[l] *Federico II University of Naples, Naples, Italy*
[m] *Bonn University Clinic, Bonn, Germany*
[n] *Montréal University, CHU Sainte-Justine, Montréal, Canada*
[o] *University of Calgary, Calgary, Canada*
[p] *Radboud University Medical Center, Nijmegen, The Netherlands*

[q] *Fundação de Hematologia e Hemoterapia de Pernambuco (HEMOPE), Recife, PE, Brazil*
[r] *Centro de Hematologia e Hemoterapia do Ceará (Hemoce), Fortaleza, CE, Brazil*
[s] *Centro de Hematologia e Hemoterapia de Santa Catarina (Hemosc), Florianópolis, SC, Brazil*
[t] *Centro de Hematologia e Hemoterapia do Paraná (Hemepar), Curitiba, PR, Brazil*

Background: Eradicating inhibitors to restore the effectiveness of Factor VIII (FVIII) is a desirable treatment goal for People with Severe Hemophilia A (PwSHA) and inhibitors, as this enables treatment of bleeding episodes with FVIII concentrates. However, since Immune Tolerance Induction (ITI) is a burdensome and costly treatment, it is important to identify determinants for ITI success to decide if it is worth undertaking ITI. For more effective treatment allocation, there is a need to identify which persons will or will not benefit from ITI. **Aim:** We aimed to identify determinants of successful ITI in PwSHA and to use these determinants in a clinical prediction model. **Methods:** German, Brazilian, Dutch, Canadian, and Italian PwSHA who underwent ITI were included. The primary outcome was clinical ITI success, defined by (1) a negative inhibitor titer, and (2) an adequate clinical response to FVIII concentrates. Clinical determinants included F8 genotype, race, age, cumulative exposure days to FVIII, inhibitor titers, and ITI regimen. Genetic determinants included in the analyses were FCGR gene, IL10 CA short tandem repeat, and gene variants. Crude Relative Risks (RR) were calculated for ITI success with 95% Confidence Intervals (95% CI). **Results:** In total, 224 PwSHA were included (61 German, 51 Brazilian, 45 Dutch, 39 Canadian, and 28 Italian). The median ages at inhibitor development and ITI start were 2-years (Interquartile Range [IQR 1–3]) and 2-years (IQR 1–6). The median interval between inhibitor diagnosis and ITI start was 17-weeks (IQR 2–64). Most ITI trials started with recombinant FVIII (130; 58%) and the median prescribed regimen at ITI start was 43 IU/kg/day (IQR 21–200). The need for adjuvant therapy and central venous access infection were related to failure, while inhibitor titer at detection < 10 BU/mL, inhibitor titer immediately before ITI start < 10 BU/mL, and peak inhibitor titer ever measured < 100 BU/mL were related to success. Inhibitor peak titer below 100 BU/mL showed the highest chance for ITI success (OR = 11.5, 95% CI 5.5–24.3, p < 0.001). **Conclusion:** Historical peak titer below 100 BU/mL was the strongest determinant for ITI success. Genetic analyses will be available by the due date, and we will develop a prediction model to estimate the chance of success.

https://doi.org/10.1016/j.htct.2024.09.944

GENOMIC DIVERSITY AND ANCESTRY OF ADMIXED PATIENTS WITH HEMOPHILIA A AND INHIBITORS: INSIGHTS FROM WHOLE EXOME SEQUENCING IN THE BRAZILIAN IMMUNE TOLERANCE (BRAZIT) STUDY

HP Santanna, R Tou, RM Camelo, L Faria, MM Dias, J Duarte, RP Souza, LW Zuccherato, E Tarazona Santos, SM Rezende

Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil

Hemophilia A is an X-linked bleeding disorder caused by mutations in the FVIII gene. BrazIT is a nationwide cohort of 193 patients that, developing neutralizing alloantibodies (inhibitors) against the first line treatment with exogenous FVIII, received Immunotolerance Treatment (ITI). Sixtyseven patients (35%) failed ITI, 62 (32%) achieved partial success, and 64 (33%) had complete success. We performed whole exome sequencing of BrazIT and estimated medians of 64%, 17%, and 13% of European, African, and Native American ancestries, respectively, based on autosome SNVs, underscoring the diversity of this cohort. After controlling for covariates, we did not observe association between these continental ancestries and inhibitor titers or ITI success, but Native American ancestry was negatively associated with large deletions in FVIII gene (β = -0.081, p = 0.011). In Latin American populations, sex-ancestry bias is the rule: during the last five centuries, European admixture has been preferentially mediated by males, while African and Native American admixture preferentially by females. We estimated X-chromosome ancestry to confirm the pervasive sex-ancestry bias in BrazIT. As expected, BrazIT individuals show Native American ancestry bias (Autosome - X-chromosome bias: 0.06, p < 0.001), but exceptionally, no African ancestry bias (-0.005, NS). This result suggests that X-chromosomes of predominant African origins are underrepresented among hemophilia patients high-responding inhibitors, exemplifying the unexplored issue of how sex-ancestry bias in Post-Columbian migrations from Europe and Africa to the Americas have differently shaped the patterns of genetic diversity of X-chromosome and autosomal linked mendelian diseases.

https://doi.org/10.1016/j.htct.2024.09.945

SWITCHING PROPHYLAXIS DURING AN IMMUNE TOLERANCE INDUCTION EVOLVING WITH FAILURE: A CASE REPORT FROM A BRAZILIAN HEMOPHILIA TREATMENT CENTER

RM Camelo [a], LCM Henriques [a], MM Dias [a], AA Garcia [b], B Cabrera [b], J Alvares-Teodoro [b]

[a] *Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, MG, Brazil*
[b] *Hemocentro de São José do Rio Preto, São José do Rio Preto, MG, Brazil*

Factor VIII (FVIII) prophylaxis is recommended to prevent bleeds in people with hemophilia A (PwHA). However, up to 30% of severe PwHA (residual plasmatic FVIII activity < 1%) develop anti-FVIII (FVIII) neutralizing antibodies (i.e., inhibitors), leading to ineffectiveness of FVIII replacement and worse outcomes. Immune Tolerance Induction (ITI) is the treatment of choice to eradicate inhibitors, but it demands frequent intravenous infusions and a higher risk of bleeding. Bypassing Agent (BpA) prophylaxis was recommended to avoid bleeding during ITI. Emicizumab is currently available as a prophylactic agent for PwHA and inhibitors, although its impact during ITI is not well described. We reported the effect