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LINHA DE PESQUISA: HEMOGLOBINOPATIAS (3 artigos)

1- British Journal of Haematology, 201(2): 343-352, 2023.

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Genome-wide association study of early ischaemic stroke risk in Brazilian individuals with sickle cell disease implicates ADAMTS2 and CDK18 and uncovers novel loci

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Ischaemic stroke is a common complication of sickle cell disease (SCD) and without intervention can affect 11% of children with SCD before the age of 20. Within the Trans-Omics for Precision Medicine (TOPMed), a genome-wide association study (GWAS) of ischaemic stroke was performed on 1333 individuals with SCD from Brazil (178 cases, 1155 controls). Via a novel Cox proportional-hazards analysis, we searched for variants

associated with ischaemic stroke occurring at younger ages. Variants at genome-wide significance ($p < 5 \times 10^{-8}$) include two near genes previously linked to non-SCD early-onset stroke (<65 years): ADAMTS2 (rs147625068, $p = 3.70 \times 10^{-9}$) and CDK18 (rs12144136, $p = 2.38 \times 10^{-9}$). Meta-analysis, which included the independent SCD cohorts Walk-PHaSST and PUSH, exhibited consistent association for variants rs1209987 near gene TBC1D32 ($p = 3.36 \times 10^{-10}$), rs188599171 near CUX1 ($p = 5.89 \times 10^{-11}$), rs77900855 near BTG1 ($p = 4.66 \times 10^{-8}$), and rs141674494 near VPS13C (1.68×10^{-9}). Findings from this study support a multivariant model of early ischaemic stroke risk and possibly a shared genetic architecture between SCD individuals and non-SCD individuals younger than 65 years.

2- Advances in Skin & Wound Care, 36(2): 98-105, 2023.

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Factors Associated with Leg Ulcers in Adults with Sickle Cell Disease in Brazil

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Objective: To define the prevalence of leg ulcers and identify the clinical and laboratory factors associated with leg ulcers in adult participants.

Methods: The authors conducted a cross-sectional study of 1,109 patients who were 18 years or older with SS or Sβ0-thalassemia genotypes from a Brazilian cohort. Investigators assessed the prevalence of factors associated with leg ulcers from 2013 to 2017.

Results: The prevalence of leg ulcers was 21%. Increasing age (odds ratio [OR], 1.07; range, 1.06-1.09), male sex (OR, 2.03; range, 1.44-2.87), treatment with chronic transfusion therapy (OR, 1.88; range, 1.15-3.03), higher indirect bilirubin levels (OR, 1.48; range, 1.02-2.16), and low hemoglobin levels (OR, 2.17; range, 1.52-3.11) were associated with leg ulcers. Participants who self-reported as Black (OR, 6.75; range, 2.63-

21.32), mixed (OR, 3.91; range, 1.55-12.20), and other/unknown (OR, 3.84; range, 1.04-15.24) were more likely to have leg ulcers compared with those who self-reported as White.

Conclusions: The prevalence of leg ulcers in this Brazilian cohort was higher than the prevalence reported in developed countries. Known factors such as age and male sex were corroborated. The increased bilirubin level and decreased hemoglobin levels among participants with leg ulcers support the hypothesis that hemolysis is correlated with leg ulcer pathogenesis. Self-reported black skin color was an independent predictor of leg ulcers and warrants further study to understand the etiology and implications of this finding.

3- Annals of Hematology, 102(5): 1019-1027, 2023.

https://doi.org/10.1007/s00277-023-05150-4

Estimated glomerular filtration rate in Brazilian adults with sickle cell disease: results from the REDS-III multicenter cohort study

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Chronic kidney disease (CKD) has a significant impact on sickle cell disease (SCD) morbidity and mortality. Early identification of individuals at highest risk of developing CKD may allow therapeutic intervention to prevent worse outcomes. This study aimed

to evaluate the prevalence and risk factors for reduced estimated glomerular filtration rate (eGFR) among adults with SCD in Brazil. Participants in the REDS-III multicenter SCD cohort with more severe genotypes aged ≥ 18 years with at least two serum creatinine values were analyzed. The eGFR was calculated using the Jamaica Sickle Cell Cohort Study GFR equation. The eGFR categories were defined according to the K/DOQI. Participants with eGFR ≥ 90 were compared to those with those with eGFR < 90. Among the 870 participants, 647 (74.4%) had eGFR ≥ 90, 211 (24.3%) had eGFR 60 to 89, six (0.7%) had eGFR 30 to 59, and six (0.7%) had ESRD. Male sex (OR: 37.3; 95%CI: 22.4-65.1), higher age (OR: 1.04; 95%CI: 1.02-1.06), higher diastolic blood pressure (OR: 1.03; 95%CI: 1.009-1.06), lower Hb (OR: 0.80; 95%CI: 0.68-0.93), and lower reticulocytes (OR: 0.94; 95%CI: 0.89-0.99) levels were independently associated with eGFR < 90. There was a trend towards higher odds of death in participants with eGFR < 90 (OR: 1.8; 95%CI: 0.95-3.32; p = 0.065). In turn, participants with eGFR < 60 had a 12.2 (95%CI: 2.1-96.9) times higher odds for death when compared to those with eGFR ≥ 60. In this study, eGFR < 90 was observed in one-quarter of adults. Older age, male sex, higher diastolic blood pressure, lower hemoglobin, and lower reticulocyte levels were associated with occurrence of eGFR < 90. Estimated GFR < 60 increased the risk of mortality.

LINHA DE PESQUISA: TRANSPLANTES, ENXERTOS E TERAPIA CELULAR (1 artigo)

1- Transfusion, 63(1): 269-271, 2023.

https://doi.org/10.1111/trf.17194

Critical failure of a cell therapy products storage tank: Description, investigation and implemented improvements

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No abstract available (Letter)

LINHA DE PESQUISA: COAGULOPATIAS (3 artigos)

1- Haemophilia, 29(2): 668-670, 2023.

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Prevalence of sporadic haemophilia A

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No abstract available (Letter)

2- Pediatric Hematology and Oncology, 2023 Feb 24;1-7.

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Changing recombinant factor VIII to plasma-derived factor VIII during immune tolerance induction

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No abstract available (Letter)

3- Viruses, 15(4): 938, 2023.

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Inflammatory Response and Activation of Coagulation after COVID-19 Infection

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SARS-CoV-2 (COVID-19) infection is responsible for causing a disease with a wide spectrum of clinical presentations. Predisposition to thromboembolic disease due to excessive inflammation is also attributed to the disease. The objective of this study was to characterize the clinical and laboratory aspects of hospitalized patients, in addition to studying the pattern of serum cytokines, and associate them with the occurrence of thromboembolic events.

Methodology: A retrospective cohort study with 97 COVID-19 patients hospitalized from April to August 2020 in the Triângulo Mineiro macro-region was carried out. A review of medical records was conducted to evaluate the clinical and laboratory aspects and the frequency of thrombosis, as well as the measurement of cytokines, in the groups that presented or did not present a thrombotic event.

Results: There were seven confirmed cases of thrombotic occurrence in the cohort. A reduction in the time of prothrombin activity was observed in the group with thrombosis. Further, 27.8% of all patients had thrombocytopenia. In the group that had thrombotic events, the levels of IL1b, IL-10, and IL2 were higher ($p < 0.05$).

Conclusions: In the studied sample, there was an increase in the inflammatory response in patients with thrombotic events, confirmed by the increase in cytokines. Furthermore, in this cohort, a link was observed between the IL-10 percentage and an increased chance of a thrombotic event.

LINHA DE PESQUISA: DOENÇAS TRANSMISSÍVEIS POR TRANSFUSÃO E TRANSPLANTE (1 artigo)

1- Transfusion. 2023, Mar 17.

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Leukoreduction as a control measure in transfusion transmission of visceral leishmaniasis

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Background: Asymptomatic visceral leishmaniasis (VL) infection is a risk for transfusion safety. Leukoreduction has been an alternative for the prevention of some blood-borne diseases, including VL. This study aimed to evaluate the role of leukoreduction of cellular blood components as a control measure for transfusional VL transmission.

Research design and methods: A total of 161 polytransfused patients with non-leukoreduced blood components (HNL), 95 polytransfused with leukoreduced blood components (LH), and 202 non-transfused (NT) from endemic regions for VL and with a

similar epidemiological profile. The detection of antibodies against VL was performed by ELISA and the presence of the parasite was investigated by real-time PCR. Statistical significance was defined as $p < .05$.

Results: When comparing three groups, ELISA results were statistically significant ($p = .0065$). The residual analysis of ELISA showed statistically significant for the HNL group compared to the general group ($p = .002$; OR: 5.6; CI: 1.7-25.8), demonstrating that individuals who received non-leukoreduced transfusions are five times more likely to acquire *Leishmania infantum* infection than the general.

Discussion: Higher prevalence in the group with HNL and low prevalence in those who received LH, similar to NT patients, highlight the risk of transfusional VL transmission and reinforce the role of leukoreduction in its prevention.