e limitações inerentes ao uso de dados secundários. Portanto, recomenda-se novas pesquisas, especialmente de natureza qualitativa e multicêntrica, que permitam compreender melhor as diferenças.

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PREDICTING RECURRENT VENOUS THROMBOEMBOLISM THROUGH PATIENT-SPECIFIC SIMULATION OF BLOOD CLOT GROWTH USING A PARTIAL DIFFERENTIAL EQUATION MODEL

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Introduction: Recurrent Venous Thromboembolism (RVTE) is a leading cause of morbidity in patients with a history of thrombotic events. Despite the availability of several clinical scores, predicting recurrence remains challenging due to inter-patient variability in thrombus formation dynamics. While Machine Learning (ML) has shown promise, most models lack physiological interpretability. In contrast, mechanistic models based on differential equations can simulate clot growth but often ignore patient-specific biological variability. To improve prediction while preserving clinical transparency, this study proposes a physiologically interpretable framework that uses patient-specific kinetic parameters to simulate clot formation through a Partial Differential Equation (PDE) model, followed by binary classification of RVTE outcomes. **Objectives:** To simulate patient-specific thrombus formation using a mechanistic PDE model, based on previously estimated kinetic parameters of the coagulation cascade, and to develop a binary ML classifier combining clot size with key clinical variables to predict RVTE recurrence. **Material and methods:** A retrospective cohort of 235 patients with a first episode of Venous Thromboembolism (VTE) was used. Patient-specific kinetic parameters were obtained from a previously optimized hybrid model, which combined an Artificial Neural Network (ANN) and a system of Ordinary Differential Equations (ODEs) to map clinical and hematological features to coagulation kinetics. These parameters were then used as inputs to a two-dimensional PDE model simulating clot growth under blood flow. The model incorporated platelet transport, biochemical reactions, and flow obstruction due to platelet aggregation. Thrombus size was computed as the proportion of simulated grid space occupied by bound platelets over a 10-minute simulation. A binary classifier was developed using four variables: patient age, D-dimer level, platelet count, and simulated clot size. Thirteen ML algorithms were evaluated using five-fold cross-validation, and model performance was assessed via area under the curve (AUC), accuracy, sensitivity, specificity, and F1-score. **Results:** Simulations using patient-specific kinetic parameters significantly improved discrimination between RVTE and non-RVTE groups, as shown by clot size distributions ($p = 0.0001$, 95% confidence). Models using standard (non-personalized) parameters showed no significant outcome separation. Among ML algorithms tested, the ANN classifier with architecture (4-2-6-1) and activation functions (satlins–tansig–satlins) achieved the highest AUC (0.956), accuracy (0.886), and F1-score (0.789) on the test set. Shapley Additive Explanations (SHAP) analysis revealed that thrombus size and platelet count were the most important predictors for diagnosing RVTE, while D- dimer levels and age were more relevant in ruling out non-RVTE cases. Results show that physiological modeling improves accuracy and clinical insight. **Discussion and Conclusion:** This study introduces a novel framework that links clinical data to thrombus growth through a patient-specific PDE model, enabling physiologically grounded RVTE prediction. By combining simulated clot size with routine clinical markers, the proposed classifier outperformed traditional ML approaches. Moreover, SHAP-based analysis ensured interpretability, reinforcing its clinical relevance. This model enables accurate recurrence risk stratification and supports personalized prevention.

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PREVALÊNCIA DE PACIENTES AMBULATORIAIS COM TTPA ENCURTADO NO HOSPITAL DE CLÍNICAS UNICAMP, NO PERÍODO ENTRE JANEIRO E MAIO DE 2025.

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Introdução: A Doença Tromboembólica Venosa (TEV) é uma condição multifatorial de grande impacto em saúde pública, associada à alta morbidade e mortalidade. Diversos estudos demonstram que valores baixos do Tempo de Tromboplastina Parcial ativado (TTPa) se correlacionam com maior risco trombótico, mesmo na ausência de causas adquiridas ou hereditárias conhecidas. A identificação precoce de indivíduos com TTPa reduzido pode ser útil como ferramenta auxiliar na estratificação de risco para TEV. Por se tratar de um exame simples, amplamente disponível e de baixo custo, surge a hipótese de seu uso em conjunto com outros fatores clínicos para avaliar a tendência à hipercoagulabilidade em pacientes ambulatoriais. **Objetivos:** Determinar a prevalência de pacientes com TTPa abaixo da razão 0,95 em uma população ambulatorial, excluindo casos com alterações hereditárias ou adquiridas que interfiram na hemostasia. **Material e métodos:** Estudo observacional, analítico e longitudinal, realizado entre janeiro e maio de 2025 no Hospital de Clínicas da Unicamp. Foram analisadas 3393 amostras de pacientes adultos atendidos em ambulatório com prescrição de TTPa. Como referência, foi utilizado o valor médio de 26,4 s, obtido à partir

de amostras de 30 doadores de sangue saudáveis (15 homens e 15 mulheres). As amostras foram processadas no coagulômetro CS2500 (Sysmex), com o reagente ACTIN FSL® (Siemens). Foram excluídas amostras com condições hereditárias/adquiridas interferentes na coagulação. Os dados foram processados e avaliados estatisticamente. **Discussão e Conclusão:** Dos 3393 pacientes, 6,51% (221) apresentaram TTPa com a razão TTPa < 0.95, São pacientes aparentemente saudáveis com tendência à hipercoagulabilidade. Esses dados reforçam a evidência de que valores baixos de TTPa podem estar associados a um estado pró-coagulante. A não exclusão por idade, sexo ou outros fatores pode representar uma limitação do estudo, porém também confere aplicabilidade prática ao resultado como triagem populacional. Foi observada uma prevalência de 6,51% de pacientes com TTPa abaixo da razão de 0.95, sem causas conhecidas de alteração da hemostasia. Esses dados sugerem que o TTPa, pela sua simplicidade e baixo custo, pode ser considerado no futuro como um marcador auxiliar de risco tromboembólico, em associação com outros fatores clínicos.

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PURINERGIC SIGNALING PATHWAYS AS A MECHANISM OF PLATELET ACTIVATION IN ANTIPHOSPHOLIPID SYNDROME

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Introduction: Platelets from patients with Antiphospholipid Syndrome (APS) are known to exhibit hyperreactivity to ADP, increased P2Y12 expression, and reduced intracellular cAMP and cGMP, suggesting enhanced purinergic signaling. The mechanisms underlying this increased platelet activation remain unclear. Since adenosine regulates platelet inhibition through elevation of cAMP via A2A and A2B receptors, impaired adenosine signaling could contribute to hypercoagulability in APS. Recent findings from our group indicate that Platelets from thrombotic Primary APS (t-PAPS) demonstrate resistance to adenosine-mediated inhibition. **Objectives:** To assess whether IgG purified from t-PAPS patients modulates platelet activation and responsiveness to adenosine. **Material and methods:** A case–control study was conducted at the Hematology and Hemotherapy Center, University of Campinas (Hemocentro-UNICAMP; Ethics approval CAAE: 70399223.0.0000.5404). Washed platelets from healthy donors were incubated either alone (n = 23), with patient- or control-derived IgG, or with purinergic agonists – adenosine or NECA (1 or 10 μM) – and stimulated with ADP (10 μM) (n=14) as appropriate. Platelet activation was assessed via flow cytometry using dual labeling for CD62P (P-selectin) and PAC-1 (activated GPIIb/IIIa) expression. The percentage of double-positive platelets was used as the activation parameter, and inhibition was expressed as the relative decrease in activation in the presence of adenosine or NECA. Statistical analyses included Friedman tests with Dunn's post hoc correction and unpaired t-tests. **Results:** Under basal conditions, incubation with IgG from controls led to a rise in dual-positive platelets compared with baseline [6.9%, IQR 4.2–12.0 vs. 4.0%, IQR 3.5 –5.2; p = 0.009], while IgG from t-PAPS patients further enhanced this response, reaching higher levels [8.6%, IQR 5.3 –13.9 vs. baseline; p < 0.0001]. Furthermore, when compared IgG P vs IgG C, IgG from t-PAPS activated more platelets (double-positive for P-selectin and PAC-1) than IgG from controls (p = 0.03; Friedman with Dunn's post hoc). Upon stimulation with ADP (10 μM), preincubation with IgG P potentiated dual-positive expression compared to ADP alone [19.1%, IQR 10.0 –33.4 vs. 7.5%, IQR 5.0–14.5; p<0.0001], whereas IgG C induced a response comparable to ADP alone [14.7%, IQR 5.6–25.1 vs. 7.5%, IQR 5.0–14.5; p = 0.11]. IgG C and IgG P, both under ADP 10 μM stimulation, exhibited similar dual-positive expression (p = 0.11). However, IgG P and IgG C showed comparable inhibitory effects. For adenosine 1 μM, inhibition was 31.5 ± 21.9% with IgG P and 31.2 ± 22.4% with IgG C (p = 0.98, unpaired t-test). At 10 μM, IgG P inhibited 38.9 ± 20.8% and IgG C inhibited 39.8 ± 20.9% (p = 0.94). With NECA, inhibition remained comparable: at 1 μM, IgG P inhibited 41.2 ± 20.5% and IgG C inhibited 34.8 ± 25.2% (p = 0.63), and at 10 μM, IgG P inhibited 49.4 ± 16.4% and IgG C inhibited 36.9 ± 27.1% (p = 0.28), indicating that patient-derived IgG did not affect adenosine-mediated inhibition of platelet activation. **Discussion and Conclusion:** IgG from t-PAPS patients enhance platelet activation in healthy donors, especially under ADP stimulation, but does not impair adenosine-mediated inhibition of platelet activation. These findings suggest that pathways beyond IgG-mediated modulation may be responsible for the adenosine resistance in t-PAPS platelets. Targeting adenosine signaling may represent a potential therapeutic avenue to mitigate platelet hyperreactivity in APS.

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