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UNIVERSIDADE ESTADUAL PAULISTA
"JÚLIO DE MESQUITA FILHO"
FACULDADE DE MEDICINA

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AVALIAÇÃO DE NETs EM PACIENTES PÓS-COVID COM TROMBOEMBOLISMO

Dissertação apresentada ao Programa de Pós-Graduação em Patologia, da Faculdade de Medicina, Universidade Estadual Paulista "Júlio de Mesquita Filho", Câmpus de Botucatu, para obtenção do título de Mestre em Ciências, área de concentração em Patologia.

Orientadora: Profa. Dra. Luciane Alarcão Dias-Melicio

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FICHA CATALOGRÁFICA ELABORADA PELA SEÇÃO TÉC. AQUIS. TRATAMENTO DA INFORM.
DIVISÃO TÉCNICA DE BIBLIOTECA E DOCUMENTAÇÃO - CÂMPUS DE BOTUCATU - UNESP
BIBLIOTECÁRIA RESPONSÁVEL: ROSEMEIRE APARECIDA VICENTE-CRB 8/5651

Dezen, Ana Laura Ortega.
Avaliação de NETs em pacientes pós-COVID com tromboembolismo / Ana Laura Ortega Dezen. - Botucatu, 2022

Dissertação (mestrado) - Universidade Estadual Paulista "Júlio de Mesquita Filho", Faculdade de Medicina de Botucatu
Orientador: Luciane Alarcão Dias-Melicio
Capes: 21102007

1. Tromboembolismo. 2. Tromboinflamação. 3. COVID-19 (Doença). 4. Neutrófilos.

Palavras-chave: COVID-19; Imunotrombose; NETs (redes extracelulares de neutrófilos); Neutrófilos; Pós-COVID.

À minha avó Dercine, por ter sido meu
exemplo de resiliência e força.

Agradecimentos

Aos meus pais, Viviane e Adalberto, por sempre acreditarem em mim, fazendo questão de me mostrar que eu sou capaz de enfrentar as adversidades que surgem ao longo do caminho e a não desistir dos meus objetivos, dando apoio e um abraço apertado sempre que necessário.

Aos meus avós que se foram, Dercine e Geraldo, que foram exemplos de força, determinação e amor. À minha avó Eliza que, apesar de suas dificuldades, sempre fazia meu dia melhor com um sorriso e um beijo, comemorando todas as minhas conquistas.

Ao Thiago, meu marido e melhor amigo, por ficar ao meu lado nos momentos de insegurança e dificuldade, sempre me encorajando a seguir em frente e me lembrando dos meus sonhos. Seu companheirismo e amor foram essenciais em cada instante da minha jornada.

À minha segunda família, Sandra, Parré, Tatá e dona Dete, que sempre esteve presente torcendo pelas minhas conquistas.

Às minhas amigas, Carolina e Maria Carolina, que participaram em todos os momentos, de longe ou perto, trazendo diversão e alegria para os meus dias.

À minha orientadora, Profª. Drª. Luciane Alarcão Dias-Melicio, por mais essa oportunidade de continuar no LIAI, desde o primeiro estágio da faculdade, e por todos os ensinamentos ao longo dos anos.

Ao nosso grupo do Laboratório de Imunopatologia e Agentes Infecciosos – LIAI, Thayná e Fernando, por terem não só contribuído com a realização desse projeto, mas por todo carinho e amizade que foi criado durante esse período, sempre apoiando uns aos outros. Levarei vocês no coração.

À toda equipe do Ambulatório da Função Pulmonar do HCFMB, pela contribuição científica e pelo acolhimento. Sem eles esse trabalho não teria se concretizado.

À equipe do Laboratório de Microscopia Confocal da UNIPEX, Leandro e Paulinha, pela contribuição nas análises, pelas conversas e por toda força.

Ao Professor Valdecir Ximenes e seu laboratório, por se colocarem sempre à disposição contribuindo com o equipamento para as análises de fluorescência.

À coordenação e administração da pós-graduação em Patologia, por estarem sempre disponíveis para me auxiliar.

Ao EAP e ao Professor José Eduardo Corrente, por toda atenção e empenho nas análises estatísticas.

À Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), processos 2018/09706-7 (com aplicação emergencial na linha de COVID-19), e 2021/13354-1.

O presente trabalho foi realizado com apoio da Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Código de Financiamento 001.

“O sucesso nasce do querer, da determinação e persistência em se chegar a um objetivo. Mesmo não atingindo o alvo, quem busca e vence obstáculos, no mínimo fará coisas admiráveis.”

- Fernando Pessoa

Resumo

O SARS-CoV-2, vírus responsável pela pandemia de COVID-19 – síndrome respiratória aguda grave, ao infectar o indivíduo, induz a ativação das respostas imunológicas e inflamatória, aumentando a quantidade de células fagocíticas - principalmente neutrófilos (PMN), assim como os níveis de citocinas pró-inflamatórias, tendo como finalidade o enfrentamento viral. No entanto, quando desreguladas, essas citocinas podem causar extensa lesão tecidual devido a indução de uma tempestade inflamatória, podendo levar o indivíduo à óbito. Acredita-se que a liberação das redes extracelulares de neutrófilos (NETs), mecanismo de eliminação de patógenos, estejam relacionadas com o agravamento da doença e formação de trombos. Estudos já demonstraram um aumento na concentração de marcadores específicos de NETs em amostras séricas e purificadas de PMN, assim como em autópsias de indivíduos acometidos pela COVID-19, indicando correlação de severidade e complicações no quadro clínico dos pacientes. Casos de tromboembolismo também se encontraram aumentados na COVID-19, mesmo naqueles indivíduos recebendo tromboprofilaxia e até mesmo em momentos posteriores à infecção aguda pelo SARS-CoV-2, associando a desregulação do estado inflamatório, a ativação plaquetária e o sistema complemento induzidos pelas NETs na COVID-19. Assim, este estudo teve como objetivo avaliar a liberação de NETs por neutrófilos humanos, *in vitro*, de pacientes pós-COVID que apresentaram ou não eventos tromboembólicos em decorrência da doença. Nossos resultados demonstram que pacientes pós-COVID, que sofreram eventos tromboembólicos devido a COVID-19, liberaram níveis mais elevados de NETs, além de apresentarem diferenças na conformação das redes. Esses resultados sugerem o importante papel modulador das NETs nos processos imunológicos, inflamatórios e vasculares devido à sua presença persistente em pacientes pós-COVID.

Palavras-chave: COVID-19, neutrófilos, NETs (redes extracelulares de neutrófilos), imunotrombose, pós-COVID.

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