

## **Malaria exposure increases plasma levels of a heart failure marker in a Brazilian endemic area**

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The ways in which malaria can impact the cardiovascular system remain unclear. We aimed to investigate whether exposure to *Plasmodium* spp. affects the risk of heart failure (HF, using NT-proBNP as a proxy marker) in the Brazilian Amazon. The study was conducted from June 2020 to August 2021, enrolling patients with lifetime exposure (n=436), no prior exposure (n=354) and active malaria (n=119). Exposure to *Plasmodium* spp. was defined through the presence of IgG against the parasite protein MSP1-19. Overlap propensity score weighting was applied to adjust for confounding variables, and then logistic regression models were performed. We evaluated clinically established NT-proBNP cut-offs for HF in outpatient settings, and included one defined by the assay detection limit. Our findings suggest that individuals exposed to *P. falciparum* had an over 2.73-fold greater chance of having NT-proBNP levels above any of the thresholds assessed. When stratified by sex, only one cut-off was significant among males, whereas all were significant for females with even higher ORs (all >4.61). No significant differences were found between those exposed to *P. falciparum* and/or *P. vivax* and those with no prior exposure, nor between PvMSP1-19 seropositive and seronegative individuals. Among patients with active malaria, higher parasitemia was also associated with increased odds of elevated NT-proBNP. For every 100-unit increase in parasitemia (infected-erythrocytes/ $\mu$ L), the odds of NT-proBNP above the cut-offs increased by at

least 1.8%. Median of parasitemia was 2905 (667, 6713) IE/ $\mu$ L. Elevated levels of NT-proBNP were found in at least 20% of patients with active malaria across all cut-offs, but decreased significantly in the follow-up, 33 (IQR 28, 37) days later. These findings suggest that malaria may affect the cardiovascular system not only during acute infection, but also after exposure to *P. falciparum*. Further investigations are necessary to clarify the mechanisms involved.