Prémio Pedro Eurico Lisboa SPD/Lilly 2021: Resumos dos Trabalhos Premiados

Pedro Eurico Lisboa SPD/Lilly Prize 2021: Abstracts of the Awarded Works

> 1º PRÉMIO

Referência

Cunha-Guimaraes JP, Guarino MP, Timóteo AT, Caires I, Sacramento JF, Ribeiro MJ, Selas M, Santiago JCP, Mota-Carmo M, Conde SV. Carotid body chemosensitivity: early biomarker of dysmetabolism in humans. Eur J Endocrinol. 2020 Jun; 182(6): 549-557.

Autores e Instituições

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Abstract

Objective: The carotid bodies (CBs) are peripheral chemoreceptor organs classically described as being O2 sensors, which are increasingly emerging as core players in metabolic control. Herein we evaluated CB activity in prediabetes patients and determined its correlation with dysmetabolism clinical features.

Design and Methods: Prediabetes patients were recruited at the Cardiology Service, Hospital Santa Marta, Centro Hospitalar Lisboa Central, EPE (CHLC-EPE). The study was approved by CHLC-EPE and NOVA Medical School Ethics Committee. Thirty-three prediabetic and 14 age-matched, non-prediabetic, volunteers had their peripheral chemosensitivity evaluated by the Dejours test. Serum biomarkers of metabolic disease, insulin sensitivity (HOMA-IR), blood pressure, carotid intima-media thickness (cIMT) and glucose tolerance were assessed.

Results: CB chemosensitivity was significantly increased in prediabetic group ($P < 0.01$). Fasting blood, glucose intolerance, fasting insulin and HOMA-IR were significantly higher in prediabetes patients. Insulin resistance correlated both with peripheral chemosensitivity, assessed by the Dejours test ($P < 0.05$) and with abdominal circumference ($P < 0.01$). HbA1c correlated with HOMA-IR ($P < 0.05$) and left cIMT ($P < 0.05$) in prediabetes patients.

Conclusions: We conclude that CB is overactive in prediabetes subjects and that peripheral chemosensitivity correlates with fasting insulin and insulin resistance representing a novel non-invasive functional biomarker to forecast early metabolic disease.

> MENÇÕES HONROSAS

Referência

Monteiro-Soares M, Boyko EJ, Jeffcoate W, Mills JL, Russell D, Morbach S, Game F. Diabetic foot ulcer classifications: A critical review. Diabetes Metab Res Rev. 2020 Mar; 36 Suppl 1: e3272.

Autores e Instituições

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Abstract

Classification and scoring systems can help both clinical management and audit outcomes of routine care. The aim of this study was to assess published systems of diabetic foot ulcers (DFUs) to determine which should be recommended for a given clinical purpose. Published classifications had to have been validated in populations of > 75% people with diabetes and a foot ulcer. Each study was assessed for internal and external validity and reliability. Eight key factors associated with failure to heal were identified from large clinical series and each classification was scored on the number of these key factors included. Classifications were then arranged according to their proposed purpose into one or more of four groups: (a) aid communication between health professionals, (b) predict clinical outcome of individual ulcers, (c) aid clinical management decision making for an individual case, and (d) audit to compare outcome in different populations. Thirty-seven classification systems were identified of which 18 were excluded for not being validated in a population of >75% DFUs. The included 19 classifications had different purposes and were derived from different populations. Only six were developed in multicentre studies, just 13 were externally validated, and very few had evaluated reliability.Classifications varied in the number (4 - 30), and definition of individual items and the diagnostic tools required. Clinical outcomes were not standardized but included ulcer-free survival, ulcer healing, hospitalization, limb amputation, mortality, and cost. Despite the limitations, there was sufficient evidence to make recommendations on the use of particular classifications for the indications listed above.

Referência

Seraphim PM, Leal EC, Moura J, Gonçalves P, Gonçalves JP, Carvalho E. Lack of lymphocytes impairs macrophage polarization and angiogenesis in diabetic wound healing. Life Sci. 2020 Aug 1; 254: 117813.

Autores e Instituições

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Abstract

Aims: This study aimed to investigate the effect of lymphocytes in wound healing and the underlying mechanisms, in diabetic and non-diabetic mice, using Balb/c recombination activating gene (Rag)-2 and interleukin 2 receptor gamma (IL-2Rγ) double knockout (KO) (RAG2−/− IL-2Rγ−/−) mice.
Main Methods: Wound healing in vivo was performed in control and STZ-induced diabetic mice, in both KO and WT mice. Inflammation and ROS production were evaluated by immunofluorescence microscopy analysis, antioxidant enzymes and angiogenesis were evaluated by quantitative PCR and immunofluorescence microscopy analysis, and wound closure kinetics evolution was evaluated by measurement of acetate tracing of the wound area.
Key Findings: Wound closure was significantly delayed in KO mice, where the M1/M2 macrophage ratio and basal ROS levels were significantly increased, while antioxidant defenses and angiogenesis were significantly decreased. Moreover, the expected increase in matrix metallopeptidase (MMP)-9 protein levels in diabetic conditions was not observed in KO mice, suggesting that the mechanisms leading to the increase in MMP-9 observed in diabetic wounds may in part be lymphocyte-dependent.
Significance: Our results indicate that lack of lymphocytes compromises wound healing independent of diabetes. The lack of these cells, even in non-diabetic mice, mimics the phenotype observed in wounds under diabetic conditions. Moreover, the combination of diabetes and the lack of lymphocytes, further impair the wound healing conditions, indicating that when the innate regulatory function is lost in these KO mice, excessive M1 polarization, poor angiogenesis and impaired wound healing are worsen.