Rev Port Cardiol. 2014;33(6):339–344

Revista Portuguesa de Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

ORIGINAL ARTICLE

Immune function of peripheral T cells in patients with venous thromboembolism or coronary artery atherosclerosis

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Received 11 July 2013; accepted 19 October 2013
Available online 5 July 2014

KEYWORDS
Immune function;
T cell;
Venous thromboembolism;
Coronary atherosclerosis

Abstract
Introduction and Objectives: Recent studies have shown that the major risk factors for arterial thrombotic diseases are closely associated with venous thromboembolism (VTE). This study aimed to investigate the expression of CD3, CD4 and CD8 in T lymphocytes, the CD4/CD8 ratio and high-sensitivity C-reactive protein (hs-CRP) levels in patients with VTE, coronary artery atherosclerosis (CAA) and healthy subjects.
Methods: A total of 82 healthy subjects, 51 VTE patients and 114 CAA patients were recruited, and the expression of CD3, CD4 and CD8 in T lymphocytes and the CD4/CD8 ratio were determined. Serum hs-CRP was also measured.
Results: Compared to healthy subjects, VTE patients had significantly reduced CD3 expression ($p=0.019$), comparable CD4 expression ($p=0.868$), significantly reduced CD8 expression ($p<0.001$) and increased CD4/CD8 ratio ($p=0.044$). However, VTE patients had comparable expression of CD3, CD4 and CD8 and CD4/CD8 ratio to CAA patients. In addition, among patients with VTE or CAA, the proportion of patients with reduced CD3+ and CD8+ T lymphocytes or increased CD4/CD8 ratio was significantly higher than in healthy subjects. In addition, hs-CRP in both VTE and CAA groups was significantly higher than in healthy subjects.
Conclusions: The antigen recognition and signal transduction activation of T cells is significantly reduced in patients with VTE or CAA, and the killing effect of T cells on pathogens, including viruses, is also significantly compromised. In addition, inflammatory and immune mechanisms are involved in the occurrence and development of venous and arterial thrombosis.

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PALAVRAS-CHAVE
Função imunológica;
Célula T;
Tromboembolismo venoso;
Aterosclerose coronária

Função imunológica das células T periféricas em doentes com tromboembolismo venoso ou aterosclerose das artérias coronárias

Resumo
Introdução e objetivos: Estudos recentes mostraram que os fatores de risco *major* das doenças trombóticas arteriais estão de forma muito próxima relacionados com a trombose venosa. Este estudo visou investigar as expressões CD3, CD4 e CD8 nos linfócitos T, a razão CD4/CD8 e a proteína reativa-C de alta sensibilidade (HsCRP) nos doentes com tromboembolismo venoso (TEV), com aterosclerose das artérias coronárias (AAC) e nos indivíduos saudáveis.
Métodos: Foi recrutado um total de 82 indivíduos saudáveis, de 51 doentes com TEV e de 114 doentes com AAC e foram determinadas as expressões CD3, CD4 e CD8 nos linfócitos T e razão CD4/CD8. Foi também determinada a HsCRP sérica.
Resultados: Quando comparados com os indivíduos saudáveis, os doentes com TEV tiveram expressões significativamente reduzidas: CD3 (p=0,019) comparável com a expressão CD4 (p=0,868) e CD8 (p<0,001) e razão CD4/CD8 (p=0,044) aumentada. No entanto, os doentes com TEV tiveram expressões CD3, CD4 e CD8 e razão CD4/CD8 comparáveis aos doentes com AAC. Além disso, os resultados mostraram, nos doentes com TEV ou AAC, a proporção de doentes com expressão CD3+ reduzida e linfócitos CD8+T ou razão CD4+/CD8+ ou razão aumentada CD4+/CD8+ significativamente aumentada, quando comparados com os indivíduos saudáveis. Além disso, a HsCRP no grupo com TEV e no grupo com AAC foi significativamente superior do que no grupo dos indivíduos saudáveis.
Conclusão: O reconhecimento do antigénio e a ativação do sinal da transdução das células T estão significativamente reduzidos nos doentes com TEV ou com AAC e o efeito mortífero das células T nos patogéneos, incluindo os vírus, está significativamente comprometido. Além disso, os mecanismos inflamatórios e imunológicos estão envolvidos na ocorrência e no desenvolvimento da trombose venosa e arterial.

List of abbreviations

AS	atherosclerosis
CAA	coronary artery atherosclerosis
CI	confidence interval
HDL-C	high-density lipoprotein cholesterol
hs-CRP	high-sensitivity C-reactive protein
LDL-C	low-density lipoprotein cholesterol
OR	odds ratio
TC	total cholesterol
TG	triglycerides
VTE	venous thromboembolism

Introduction

Previously, venous thromboembolism (VTE) was regarded as a separate disease from arterial thromboembolism.[1] However, this hypothesis has been challenged. In 2003, Prandoni et al.[2] reported that transient venous thrombosis patients had more atherosclerotic plaques in the carotid arteries, suggesting that atherosclerosis can cause venous thrombosis or that the two conditions share risk factors. In the *Lancet* in 2007, Srensen et al.[3] assessed the hospitalization rate due to acute arterial cardiovascular events over 20 years in a cohort of venous thrombosis patients, and found that VTE patients had significantly increased risk for cardiovascular events. In 2008, a meta-analysis on the correlation between cardiovascular risk factors and VTE showed that the major risk factors for atherothrombotic disease were significantly associated with VTE.[4] It has been suggested that cardiovascular risk factors are also directly involved in the pathogenesis of VTE. To further investigate the potential mechanisms underlying this correlation, it would be helpful to elucidate the pathogenesis of VTE and to screen high-risk subjects for primary and secondary prevention of VTE. On the basis of previous findings, this study was undertaken to compare T-cell immune function in VTE patients, CAA patients and healthy controls, to elucidate whether inflammatory immunity is involved in the occurrence and development of venous thrombosis as in atherosclerosis. We further investigated T-cell immune function, hs-CRP and cardiovascular risk factors in VTE patients, CAA patients and healthy controls, and also evaluated the correlation between VTE and arterial thrombosis, aiming to explore the pathogenesis and risk factors of VTE.

Methods

Subjects

A total of 51 inpatients with clinically proven VTE but without CAA were recruited from the Affiliated Tongji