Population pharmacokinetic characteristics of tacrolimus in Chinese Han lung transplant recipients and optimisation of dosing regimen

Shouning Zhou[1], Qiaoyan Lian[1], Hui Xie[1], Yan-ping Guan[2], Jianxing He[1], Li Wei[1], and Chunrong Ju[1]

[1]First Affiliated Hospital of Guangzhou Medical University
[2]Sun Yat-Sen University

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Abstract

Aim: To establish a population pharmacokinetic model and optimise tacrolimus dosing regimens in Chinese Han lung transplant recipients. Methods: Tacrolimus trough concentrations and clinical data of 70 adult lung transplant recipients were collected. Population pharmacokinetic analysis was performed using a nonlinear mixed effects model. A Monte Carlo simulation was conducted to determine the optimal dosing regimen. Results: The pharmacokinetics of tacrolimus could be best described by a one-compartment model, with the CYP3A5 genotype, haematocrit (HCT), and alanine transaminase (ALT) as significant covariates. The clearance of tacrolimus in the CYP3A5 rapid and intermediate metabolisers were 3.03 and 1.99 times higher than those of CYP3A5 poor metaboliser, respectively. When HCT decreased from 0.30 to 0.20, the clearance of tacrolimus increased by 31.14%, and the apparent volume of distribution increased by 28.58%. The clearance of tacrolimus decreased by 8.67% when ALT increased from 20 IU·L-1 to 40 IU·L-1. Monte Carlo simulation indicated that recipients with CYP3A5*1/*1 receiving 3.5 mg twice daily, recipients with HCT $<$ 0.2 receiving 5 mg twice daily, and recipients with ALT $<$ 4IU·L-1 received 3 mg twice daily, could achieve the target concentrations of 10–15 ng·mL-1. Conclusions: A population pharmacokinetic model of tacrolimus in Chinese Han lung transplant recipients was successfully constructed. Recipients with the CYP3A5*1/*1 genotype, low HCT value, and low ALT value after surgery needed a higher maintenance dose to reach the therapeutic window, which provided a reference for the formulation of individualised tacrolimus regimen.

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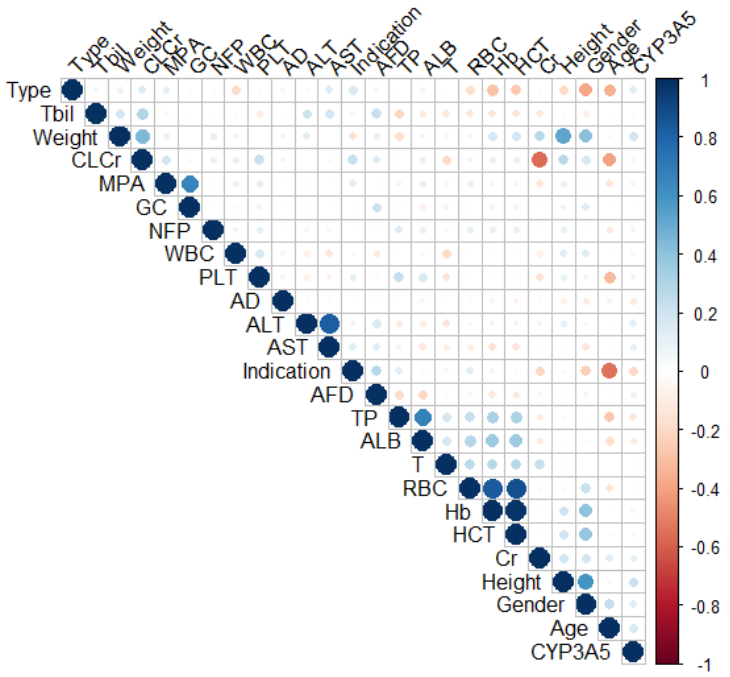

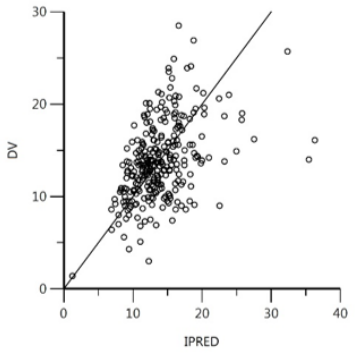

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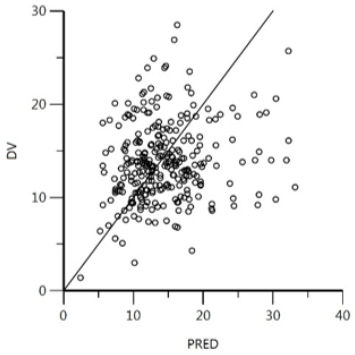

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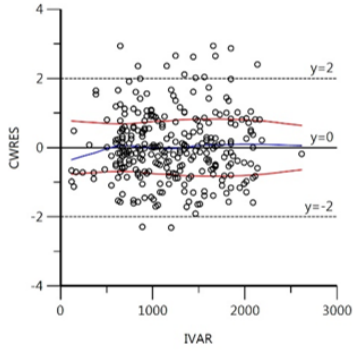

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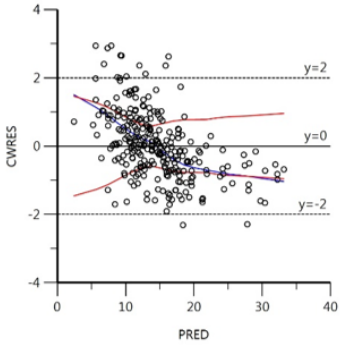

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