




# Tacrolimus pharmacogenetics in determining optimal tacrolimus dose after heart transplantation – a literature review

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**Introduction:** Tacrolimus is a cornerstone of modern immunosuppressive regimen after heart transplantation. Optimizing its use is crucial to increase effectiveness and reduce potential harm.<sup>1-3</sup> This paper aimed to present key insights into the pharmacogenetic profile of crucial cytochrome P450 (CYP) enzymes and ABC transporters involved in tacrolimus metabolism.

**Materials and Methods:** This study involved search and review of relevant literature in PubMed and PharmGKB database using keywords: heart transplantation, immunosuppressive therapy, tacrolimus, pharmacogenetics, pharmacogenomics, CYP3A4, CYP3A5, polymorphism and pharmacoconomics.

**Results:** A systematic review of the literature established links between gene polymorphisms and tacrolimus metabolism. Whether therapeutic drug monitoring could be replaced by routine pharmacogenetic testing to adjust tacrolimus dosing more efficiently is still debated. Currently, the metabolizer phenotype CYP3A5 \*1/\*1 or \*1/\*3 is the only one with official guidelines, indicating these patients may need a 1.5 to 2-fold dose increase to achieve therapeutic levels. These guidelines are published by Clinical Pharmacogenetics Implementation Consortium (CPIC). Other referent scientific societies have similar guidelines. Among Caucasians, 3-15 % are CYP3A5 expressors (\*1 carriers).

**Conclusion:** Further research is required to assess the cost-effectiveness of routine pharmacogenetic testing in clinical practice, considering its potential to prevent side effects and drug inefficacy. While pharmacogenetic testing provides valuable dosing insights, it should complement other clinical and laboratory tools in a multidisciplinary approach that includes the clinical pharmacist as part of the team.

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## LITERATURE

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