

Towards Precision Medicine: Alteplase versus Tenecteplase for Acute Ischemic Stroke

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Abstract— Despite the recent success in genomic studies in stroke, how the patient’s genes affect the responses to drugs and treatments has seldom been studied. This study performed pharmacogenomics analysis on stroke thrombolytics using an evidence-based approach, artificial intelligence, and domain experts’ knowledge.

Clinical Relevance— This study presents a modified stroke management pathway with the assistance of genomics and artificial intelligence-based analysis.

I. INTRODUCTION

Despite the success of genome-wide association studies in stroke, the second leading cause of death worldwide [1], how genes affect the responses to drugs and treatments has seldom been studied. In acute stroke management, how to select the appropriate thrombolytic agent, alteplase (tPA) versus Tenecteplase (TNK), to avoid severe adverse reactions, such as hemorrhagic transformation (HT), needs to be addressed. This paper presents a whole genome sequencing (WGS) approach to demonstrate the correlation between HT and thrombolytics, providing more precise therapeutic targeting with artificial intelligence and pharmacogenomics [2].

II. METHODS

Three methods were developed using WGS data to analyze the association between genes and drugs. First, a knowledge base construction framework with intelligent bibliometrics was utilized to recommend a top 5 gene list. Second, a graph neural network (GNN) investigated the association using protein-protein interactions with graph presentation. Lastly, domain experts conducted a manual search to create a gene list using bioinformatics results of the genes and thrombolytics.

III. RESULTS

The top 5 gene lists, shown in Fig 1, were generated to illustrate the associations between HT and thrombolytics. MMP genes were called in both data-driven methods; however, the domain experts considered that MMP9 is not associated with HT. Compared with the first two methods, manual search presented more new genes, which could result from human bias. Therefore, we recommend combining the three methods for practical use.

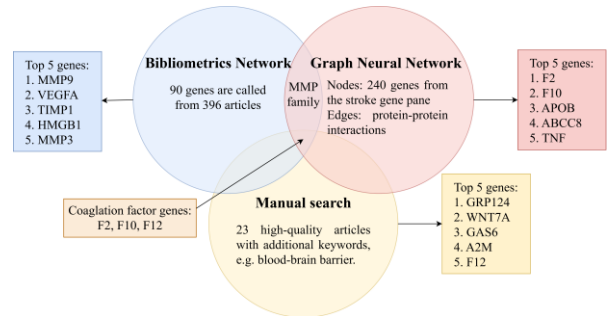


Figure 1. A Venn diagram: three proposed methods and the gene lists

IV. DISCUSSION & CONCLUSION

The gene lists generated can be used as an assistive tool to guide clinicians in choosing the more appropriate thrombolytics to avoid several adverse reactions. Compared with the current standard stroke management pathway, shown in Fig 2., WGS adds value in thrombolysis decision-making and helps in pre-, acute, and post-stroke management.

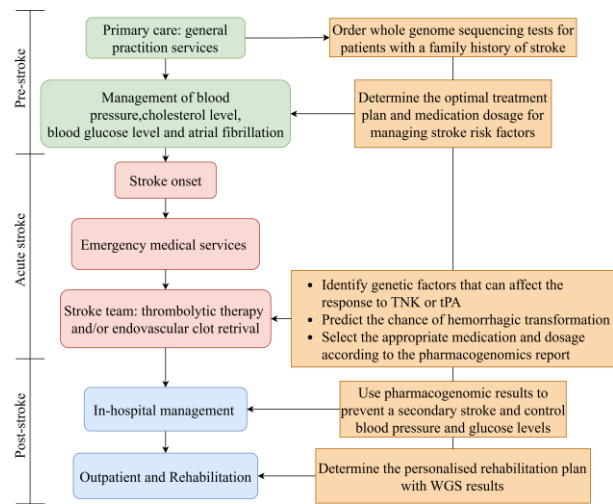


Figure 2. A modified acute ischemic stroke management with whole genome sequencing technology.

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