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Hierarchically Optimal Classification Tree Analysis of Adverse Drug Reactions Secondary to Warfarin Therapy

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Identification and detection of adverse drug reactions (ADRs) is critical to patient safety improvement, and warfarin is a medication known to be associated with a high rate of ADRs. Hierarchically optimal CTA was used to predict ADRs attributable to medications taken in addition to warfarin, for a sample of 2,289 hospital in-patients. A model involving five medications was identified, with relatively high ADR rates identified for patients, already on warfarin, who also received zolpidem tartrate, tamsulosin HCL, famotidine, nitroglycerin, and rofecoxib. The CTA model achieved moderate classification accuracy (ESS=38.0), correctly classifying 1,323 of 2,246 patients (58.9%) without an ADR, and 34 of 43 patients (79.1%) experiencing an ADR.

Data were collected from June 2000 through November 2001 at a private teaching hospital in downtown Chicago. Information on ADRs was collected by Pharmacy as part of the in-house ADR program which involves examination of caregiver reports, surveillance, and medical record reviews.

CTA[1,2] was used to predict ADR using only binary indicators of additional medications taken concurrently to warfarin. The CTA model enumerated more than one billion systems of linear inequalities, requiring ten CPU-hours to solve using a 650 MHz Pentium-4 micro-computer. Summarized in Table 1, the model identified five medications associated with a relatively high, statistically reliable ADR rate. The roster begins with the root attribute and works down the tree—which consisted of a single branch emanating from zolpidem tartrate.

Table 1: Medications identified by CTA which are associated with significant ADRs when taken concurrently with Warfarin

Medication	Ratio	%	*p*<	ESS
Zolpidem Tartrate	12/304	3.95	0.01	14.9
Tamsulosin HCL	5/72	6.94	0.004	12.7
Famotidine	10/409	2.44	0.05	17.3
Nitroglycerin	4/106	3.77	0.022	18.2
Rofecoxib	3/66	4.55	0.016	20.4

Note: Ratio = number of ADRs / number of patients with indicated medication.

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Using only information about the medications administered after the patient was admitted to the hospital, the CTA model reveals that nearly 80% of the ADRs involving warfarin occurred in approximately 40% of the patients, those receiving one (or more) of five additional medications.

References

[1]Soltysik RC, Yarnold PR (2010). Automated CTA software: Fundamental concepts and control commands. *Optimal Data Analysis, 1*, 144-160.

[2]Yarnold PR (2013). Initial use of hierarchically optimal classification tree analysis in medical research. *Optimal Data Analysis*, 2, 7-18.

Author Notes

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