

MEDICATIONS AND GENE INTERACTIONS IN THE DELIRIUM PATIENTS

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BACKGROUND

Cytochrome P450 metabolism is typically responsible for converting medications to compounds that are more water-soluble and more easily excreted. Genetic variations of cytochrome P450 enzymes may affect metabolism of medications, manifesting phenotypically as ranging from “poor” to “extensive” metabolizers. The P450 enzyme families with major CYP genetic polymorphisms are CYP2D6, CYP2C19, and CYP2C9. Medications themselves may also affect the activity of these enzymes, producing complex interactions between an individual’s P450 enzyme activities and drugs that modify those activities. Both mechanisms may contribute to medication-induced delirium.

OBJECTIVE

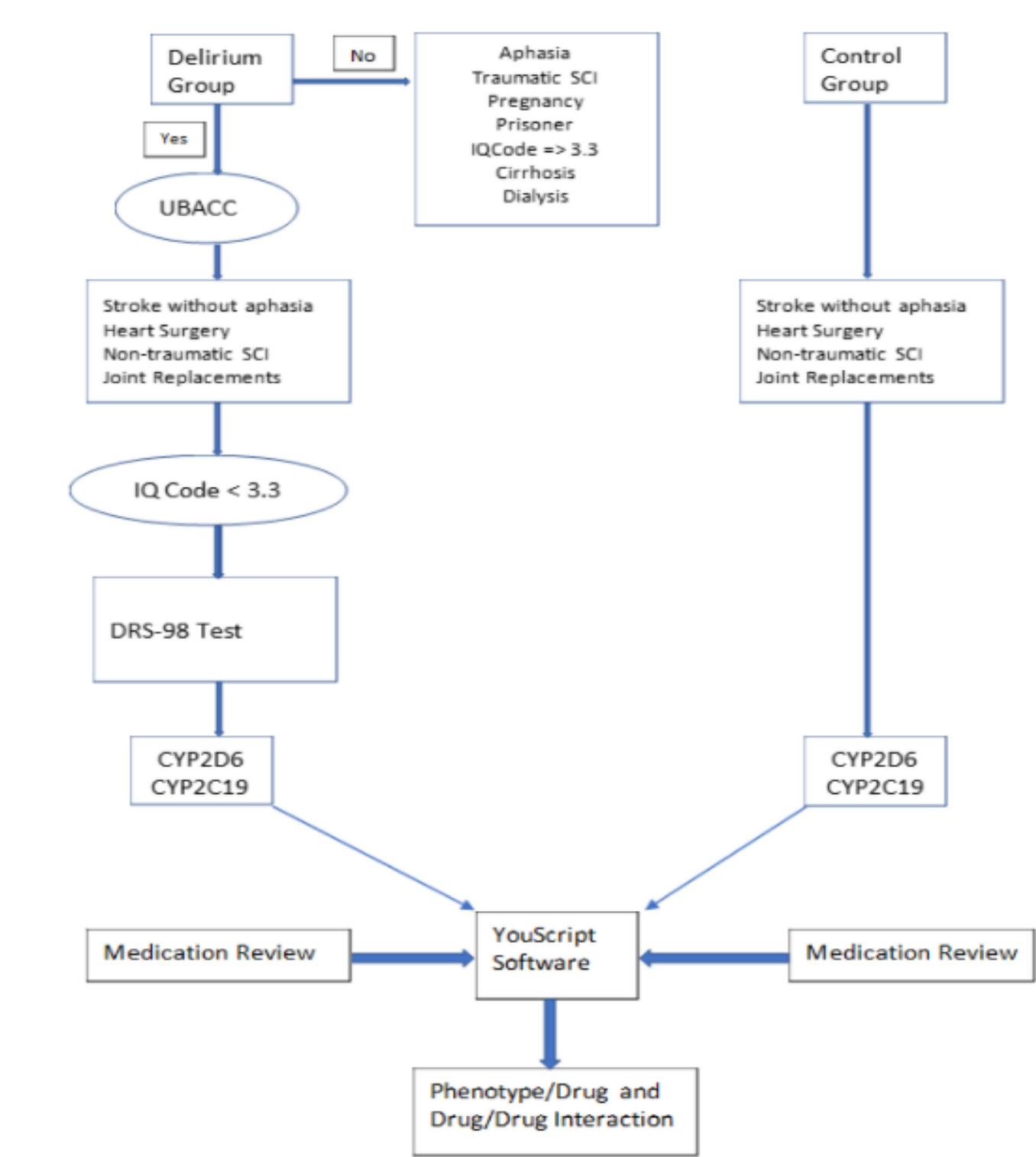
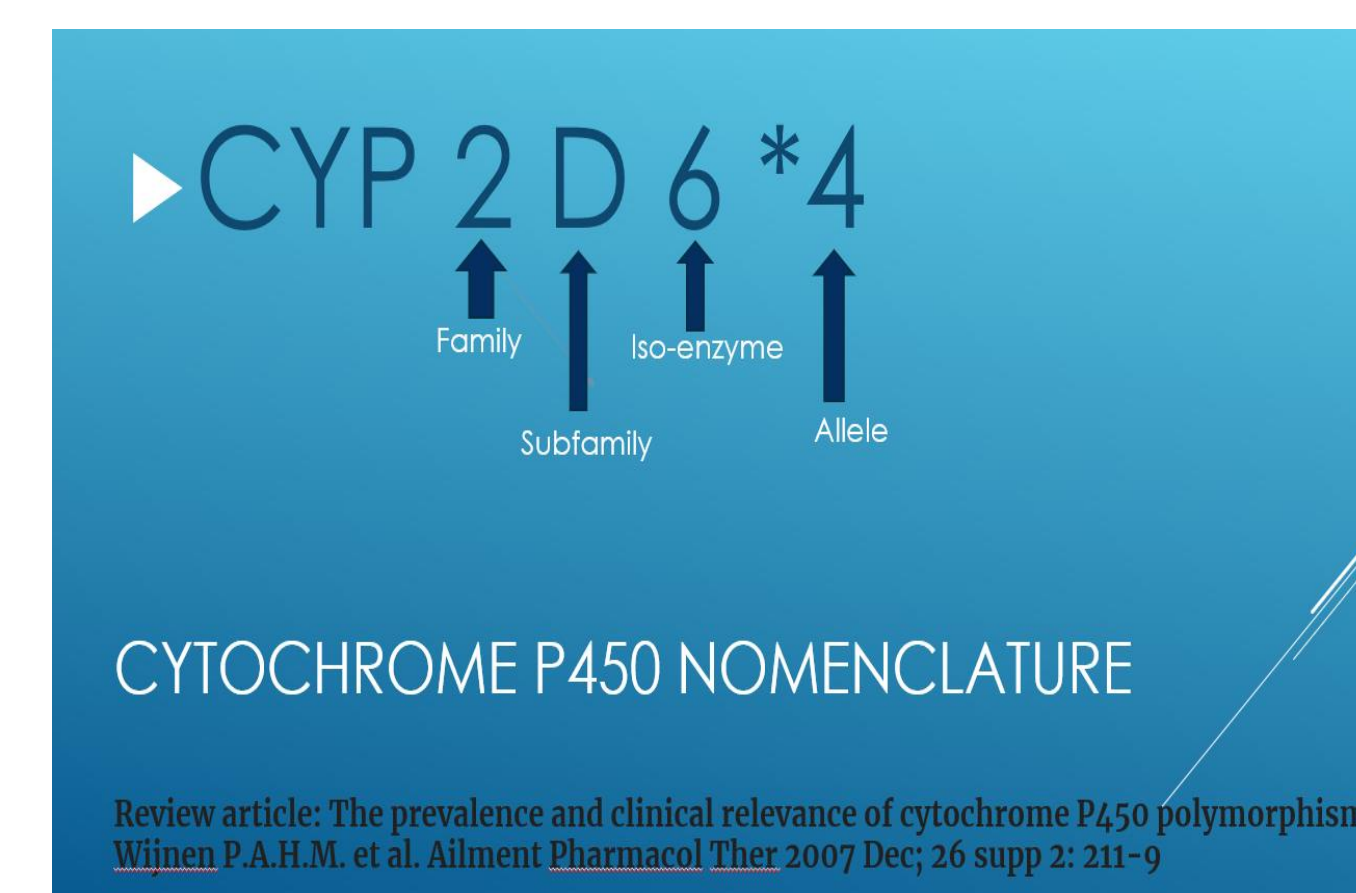
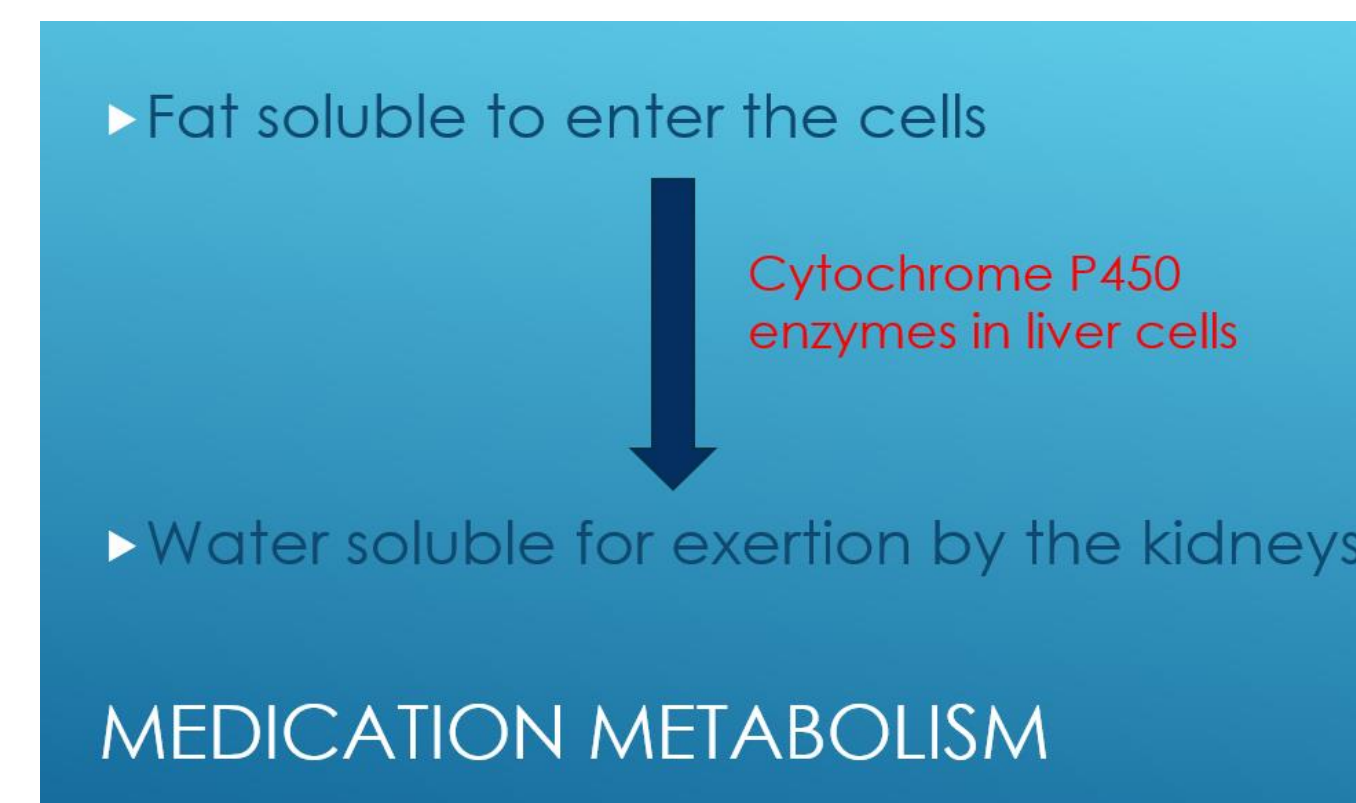
Objective of the study was to examine whether patients with delirium have higher prevalence of cytochrome-P450 drug-phenotype interactions compared to patients without delirium

METHODS

Study sample included 13 patients (8 patients in a delirium group and 5 patients in a control group). Patients were included if they had diagnosis of a stroke without aphasia, non-traumatic spinal cord injury or cardiac surgery. Study duration was from February 2019 to June 2020. Interventions included UBACC decision capacity tool, Short IQ Code dementia screening, DRS 98 delirium severity assessment, blood samples for cytochrome CYP2D6 and CYP2C19 isoenzymes genetic testing.

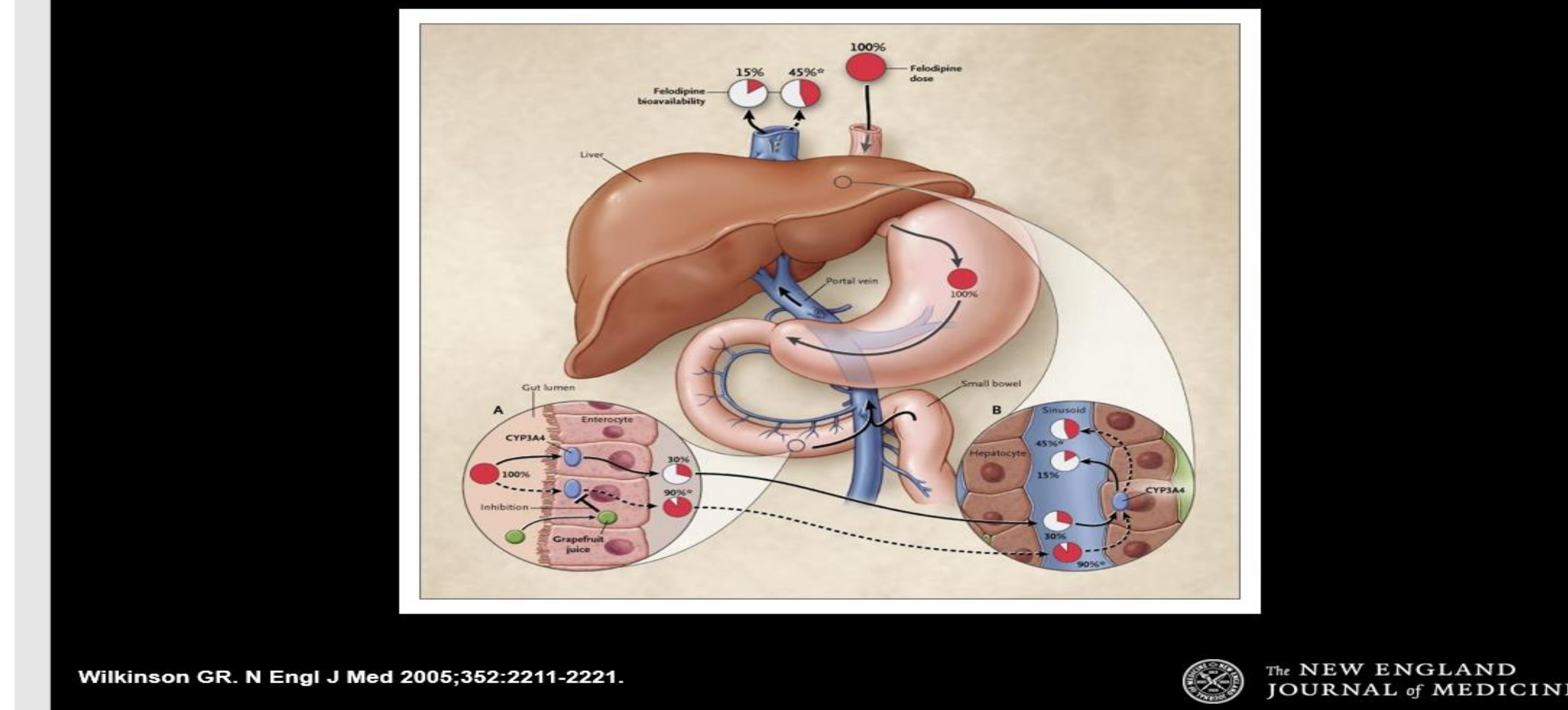
RESULTS

We identified two patients in the delirium group with CYP2D6 drug-phenotype interaction due to metoprolol. In addition, one patient in delirium group had fluoxetine and metoprolol drug-drug interaction. There were no control subjects with drug-phenotype or drug-drug interaction associated with metoprolol.



Diagnosis	Delirium Group/Patient #	Control Group/Patient #
CVA without aphasia	1	2
CVA without aphasia	6	5
CVA without aphasia	7	8
CVA without aphasia	9	
CVA without aphasia	10	11
CVA without aphasia	13	
Non-Traumatic SCI	12	
Joint Replacement	N/A	N/A
Cardiac surgery	3	4

First-Pass Metabolism after Oral Administration of a Drug, as Exemplified by Felodipine and Its Interaction with Grapefruit Juice.



Patient #	Group	CYP2D6	Phenotype	CYP2C19	Phenotype
1	Delirium	*4/*10	Intermediate metabolizer	*12/*12	Ultra-rapid metabolizer
2	Control	*4/*5	Poor metabolizer	*1/*1	Extensive metabolizer (normal)
4	Control	**2/*41 DUP	Extensive metabolizer (normal)	*1/*1	Extensive metabolizer (normal)
5	Control	*1/*2	Extensive metabolizer (normal)	*1/*1	Extensive metabolizer (normal)
8	Control	*2/*2	Extensive metabolizer (normal)	*2/*2	Poor metabolizer
11	Control	**2/*41	Extensive metabolizer (normal)	*1/*12	Ultra-rapid metabolizer

Patient #	Group	CYP2D6	Phenotype	CYP2C19	Phenotype
1	Delirium	*4/*10	Intermediate metabolizer	*12/*12	Ultra-rapid metabolizer
1	Delirium	*4/*41	Intermediate metabolizer	*1/*1	Extensive metabolizer (normal)
6	Delirium	*4/*4	Poor metabolizer	*1/*1	Extensive metabolizer (normal)
7	Delirium	*1/*2	Extensive metabolizer (normal)	**2/*2	Poor metabolizer
8	Delirium	*2/*2	Extensive metabolizer (normal)	*1/*12	Ultra-rapid metabolizer
10	Delirium	**1/*12	Extensive metabolizer (normal)	**1/*1	Extensive metabolizer (normal)
11	Delirium	*2/*2	Extensive metabolizer (normal)	*1/*2	Intermediate metabolizer
11	Delirium	Failed		*1/*12	Ultra-rapid metabolizer

Patient Number	Group	Diagnosis	Phenotype	Medication	Medication
3	Delirium	Cardiac	CYP2D6 Intermediate	Metoprolol*	Tamsulosin**

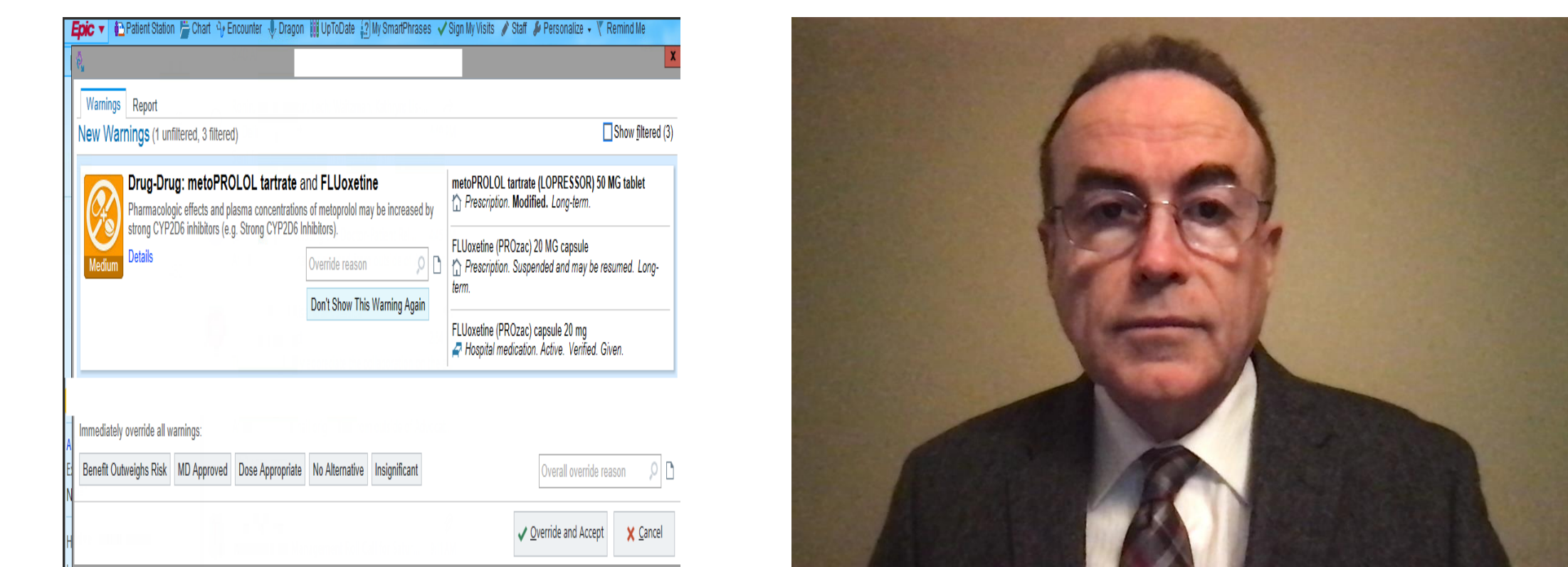
Patient Number	Group	Diagnosis	Phenotype	Medication
2	Control	CVA	CYP2D6 Poor	Carvedilol***
8	Control	CVA	CYP2C19 Poor	Fluoxetine**

CYP2D6 Metabolism	Name of the Beta Blocker
High	Metoprolol
Moderate	Propranolol
Moderate	Nebivolol
None	Atenolol
Glucuronosyltransferase	Labetalol

CYP2D6 Inhibition	Name of the SSRI
Stronger	Paroxetine
	Fluoxetine
	Duloxetine
	Escitalopram
Weaker	Sertraline

CONCLUSIONS

Cytochrome P450 genotyping and phenotyping may play a role in the prevention of delirium by providing additional information to guide safer medication prescribing. We shared results of the study with the Pharmacy Department at Lutheran General Hospital, Advocate Aurora Health. As a result of this communication there is a systemwide warning in Epic electronic medical records software against prescribing a lipid soluble beta blocker Metoprolol in combination with strong cytochrome P450 inhibiting serotonin reuptake inhibitors, like Fluoxetine.



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The authors would like to thank the Russell Center for Research and Innovation for contributing support via protocol development, statistical analysis, data collection, and funding through the Russell Research Grants programs, as well as the Advocate Charitable Organization, for their generous financial support of this study.