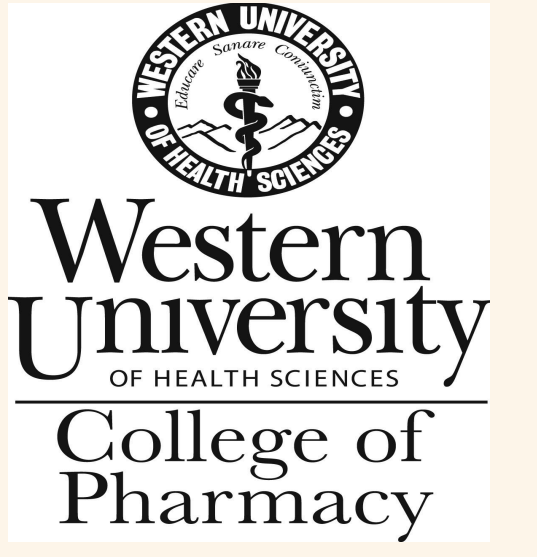


The Importance of EKG Monitoring in Geriatric Patients at Risk of Polypharmacy-Induced QTc Prolongation



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BACKGROUND

Polypharmacy, the concurrent use of multiple drugs by a patient for one or more conditions, is rising as the population ages¹. One potential adverse event of polypharmacy is a prolonged QT interval, which reflects the total duration of ventricular myocardial repolarization². A QTc interval, the QT interval corrected for heart rate from an electrocardiograph (EKG), holds clinical significance when prolonged because it is a risk factor for a life-threatening polymorphic ventricular tachyarrhythmias called torsade de pointes (TdP)². According to the Agency for Healthcare Research and Quality, 543,000 adults over the age of 65 were hospitalized for an irregular heartbeat in 2009. Most sudden cardiac deaths, ~300,000 per year in the US, are caused by ventricular arrhythmias³.

Despite these alarming statistics, it is important to note that drug-induced QT prolongation is a modifiable risk factor for TdP. Therefore, its detection/prevention via EKG monitoring and pharmacotherapeutic adjustments is of particular importance in geriatric patients, who exhibit a progressive QT prolongation with age⁴. According to the Centers for Medicare and Medicaid Services, over 25% of patients in nursing facilities in the US receive antipsychotic (AP) medications, one of many non-cardiac classes of medications that have been identified by regulatory agencies to potentially lengthen the QT interval.

Currently, literature identifying pharmacists' role in monitoring and reducing drug-induced QT prolongation is limited. Therefore, the goal of this research is to identify the impact pharmacists can have on reducing QT prolongation through medication review and provider suggestions. It also provides information to health care professionals about the importance of EKG monitoring practices in elderly patients with increased risk of QT prolongation.

STUDY OBJECTIVES & HYPOTHESIS

OBJECTIVE: The primary objective is to determine the impact of pharmacist recommendations on the potential prevention of cardiac complications, as measured by a reduction in elevated QTc interval, for patients engaged in polypharmacy. The secondary objective is to determine the pattern or frequency of EKGs on file and pharmacists recommendations made.

Hypothesis: Most residents may not have EKG records on file. For those that have an elevated QTc interval >450 msec for which providers accepted pharmacist recommendations to either decrease, change or discontinue medication, there will be a reduction in QTc interval per follow-up EKG.

METHODS

Institutional review board approval was obtained by Western University of Health Sciences. This retrospective chart review was done at Los Angeles Jewish Home for the Aging (LAJHA), a 239-bed long-term skilled nursing facility via the *Achieve Matrix* software. An initial query was performed to identify all patients taking antipsychotics with some risk of QTc prolongation. 81 patients were retrieved and their charts were reviewed to further identify patients who were on at least 1 antipsychotic during 01/01/2015 - 12/31/15. Patients were excluded if no data was available or if they expired prior to 2015. Patients included met the following criteria: 1) concurrently taking ≥ 2 QTc prolonging medications with at least 1 being an antipsychotic, 2) ≥ 70 years old, 3) have an EKG on file indicating elevated QTc ≥ 450 msec, and 4) a pharmacist recommendation present. Only 4 of 81 patients retrieved met the initial inclusion criteria to assess the primary objective, therefore chart review and sub-analysis was done on a total of 31 patients who were on ≥ 2 QTc prolonging medications, with at least 1 being an antipsychotic, and ≥ 70 years old. Data collected included demographics, medications, comorbidities, number of EKGs on file, QTc intervals if available, and details of pharmacist recommendations and provider responses. To maintain consistency, CredibleMeds® list was used to identify medications for which there is a known, conditional, or potential risk of QTc prolongation.

Fisher's exact tests, chi-square, ANOVA and t tests were used for statistical analysis and conducted using *GraphPad R Prism*® and *Microsoft Excel*®. P-values were considered statistically significant at $p < 0.05$.

RESULTS

Characteristics (QTc in msec)	QTc ≥ 450 (n=9)	QTc <450 (n=8)	No EKG (n=14)	P-Value
Gender				
Male	2 (22%)	3 (37.5%)	11 (78.6%)	0.02
Female	7 (77.8%)	5 (62.5%)	3 (21.4%)	0.02
Average Age (years)	92.4 \pm 8.63	87.38 \pm 4.60	97.07 \pm 4.25	0.16
Caucasian of Non-Hispanic Origin	9 (100%)	8 (100%)	14 (100%)	0.99
Average # of QTc Medications	2.55 \pm 1.01	2.88 \pm 0.83	3.43 \pm 1.55	0.48
PCP	1	0	1	0.64
Psych	8	8	13	0.64
Medical Conditions				
Schizophrenia	0	1	0	0.23
CKD	5	3	3	0.25
Arrhythmia	3	4	7	0.70
CAD	2	0	0	0.07
CHF	2	3	3	0.68
Allergic Rhinitis	0	2	1	0.20
Angina	2	2	0	0.15
Infection	3	1	3	0.59
HLD	3	4	9	0.35
HTN	6	7	7	0.21
Cancer	1	3	2	0.32
Dementia	3	3	7	0.70
Depression	1	2	7	0.13
GERD	6	4	8	0.77
Stroke	1	0	1	0.61
MI	0	1	0	0.23
DM 2	4	4	6	0.95
Colitis	1	0	1	0.64

Table 1. Baseline characteristics and demographics between patients with elevated QTc, non-elevated QTc, and no EKG on file.

% Distribution of Drugs by Risk Category	QTc ≥ 450 n=22	QTc <450 n=23	No EKG n=46	p-value
Known Risk for QTc	7 (31.82%)	6 (26.09%)	10 (21.74%)	0.76
Conditional Risk for QTc	13 (59.9%)	12 (52.17%)	27 (58.70%)	0.5
Potential Risk for QTc	2 (9.09%)	5 (21.74%)	6 (13.04%)	0.48

Table 2. Distribution of Medications by Risk Category as Established by Credible.Meds. Difference between distribution of medications by risk category amongst groups were not significant showing that patients that were not undergoing monitoring were are similar risk of QT prolongation as to those patients who had elevated QTc intervals.

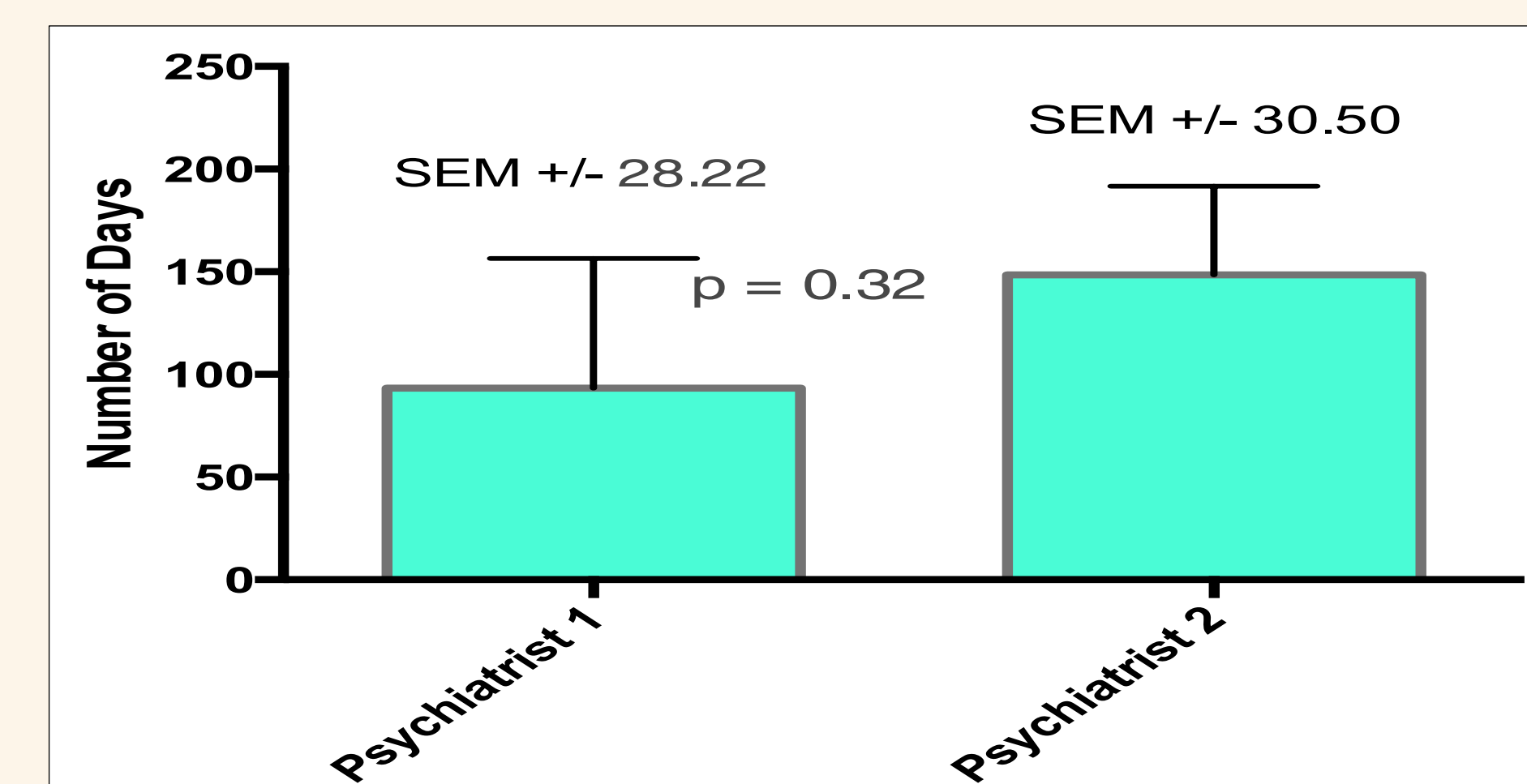


Figure 3. Comparison of the average time lapse between pharmacist recommendation and response between two psychiatrists among patients with elevated QTc intervals. There was no significant difference seen between psychiatrists when comparing the number of days taken to respond to pharmacist recommendation.

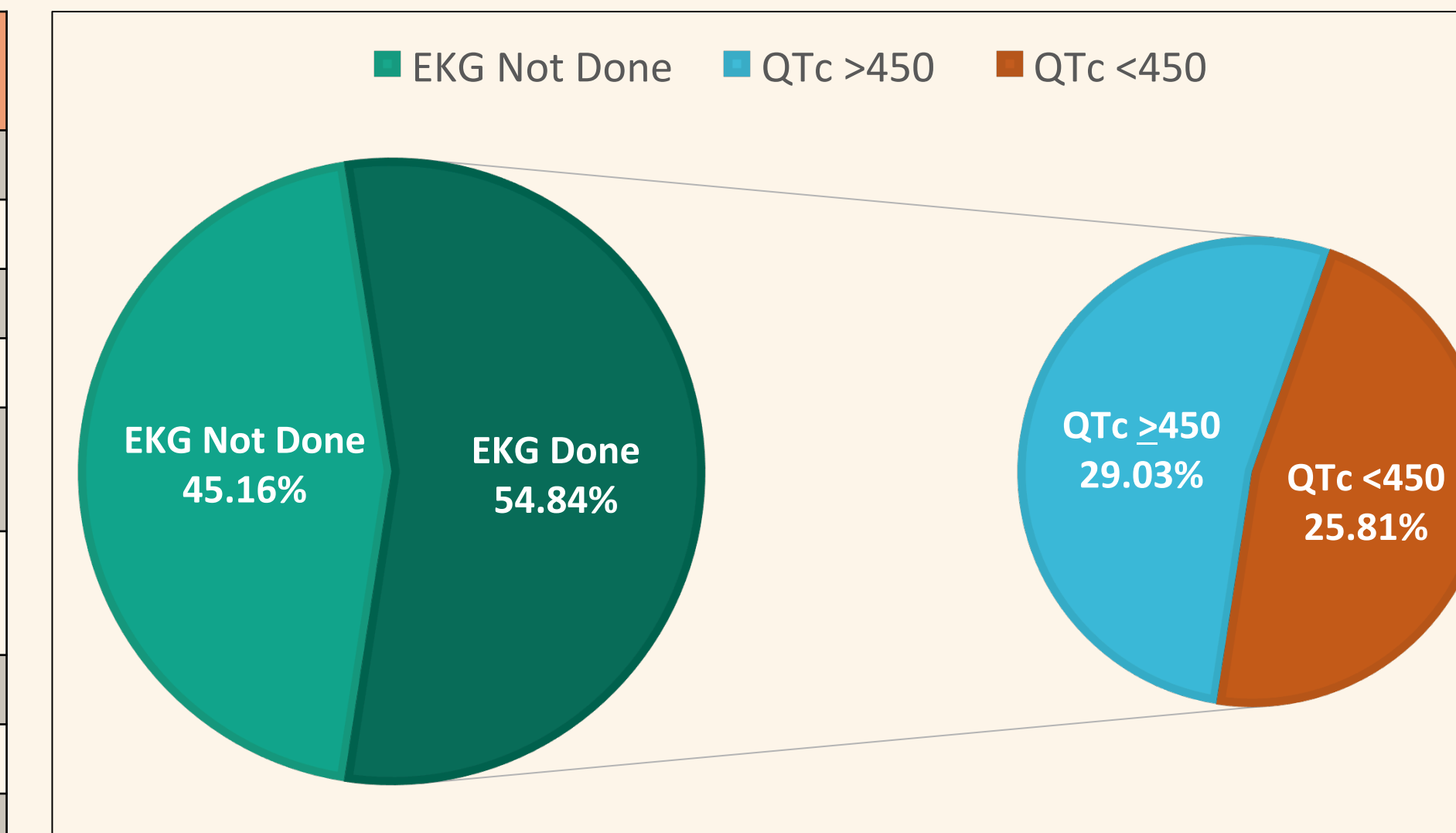


Figure 1. Percentage of EKGs Performed on Patients Taking at Least 2 or More QTc Prolonging Medications. Nearly half of patients (45.16%) with some risk of QTc prolongation from polypharmacy did not have EKGs done.

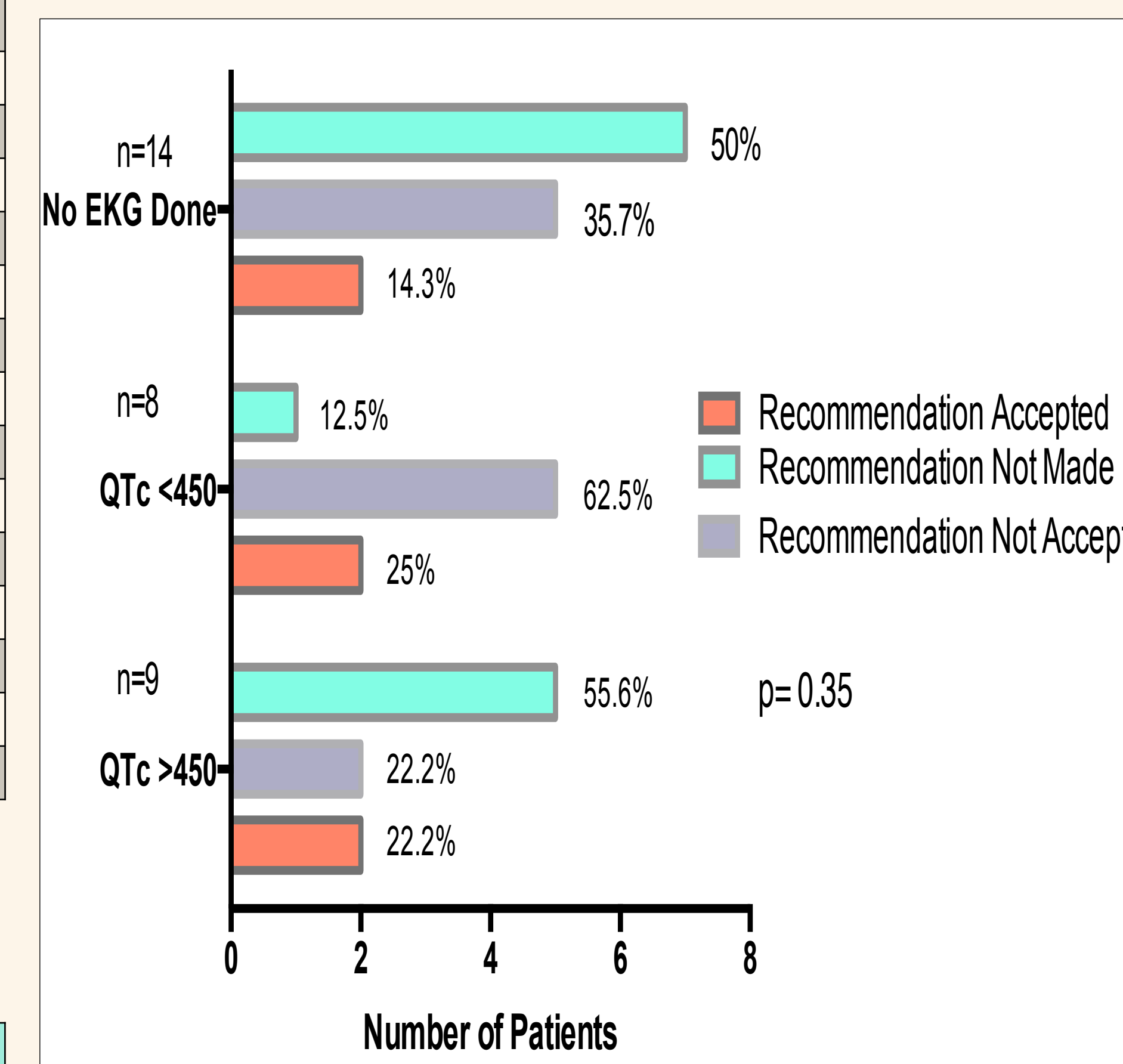


Figure 2. Analysis of EKG Status vs Pharmacist Recommendation Status. There were no significant differences in a sub-analysis looking at the number of recommendations made/accepted, made/not accepted, and not made vs those that had elevated QTc intervals, non-elevated QTc intervals, and no EKG done ($\chi^2=4.46$ $p = 0.35$).

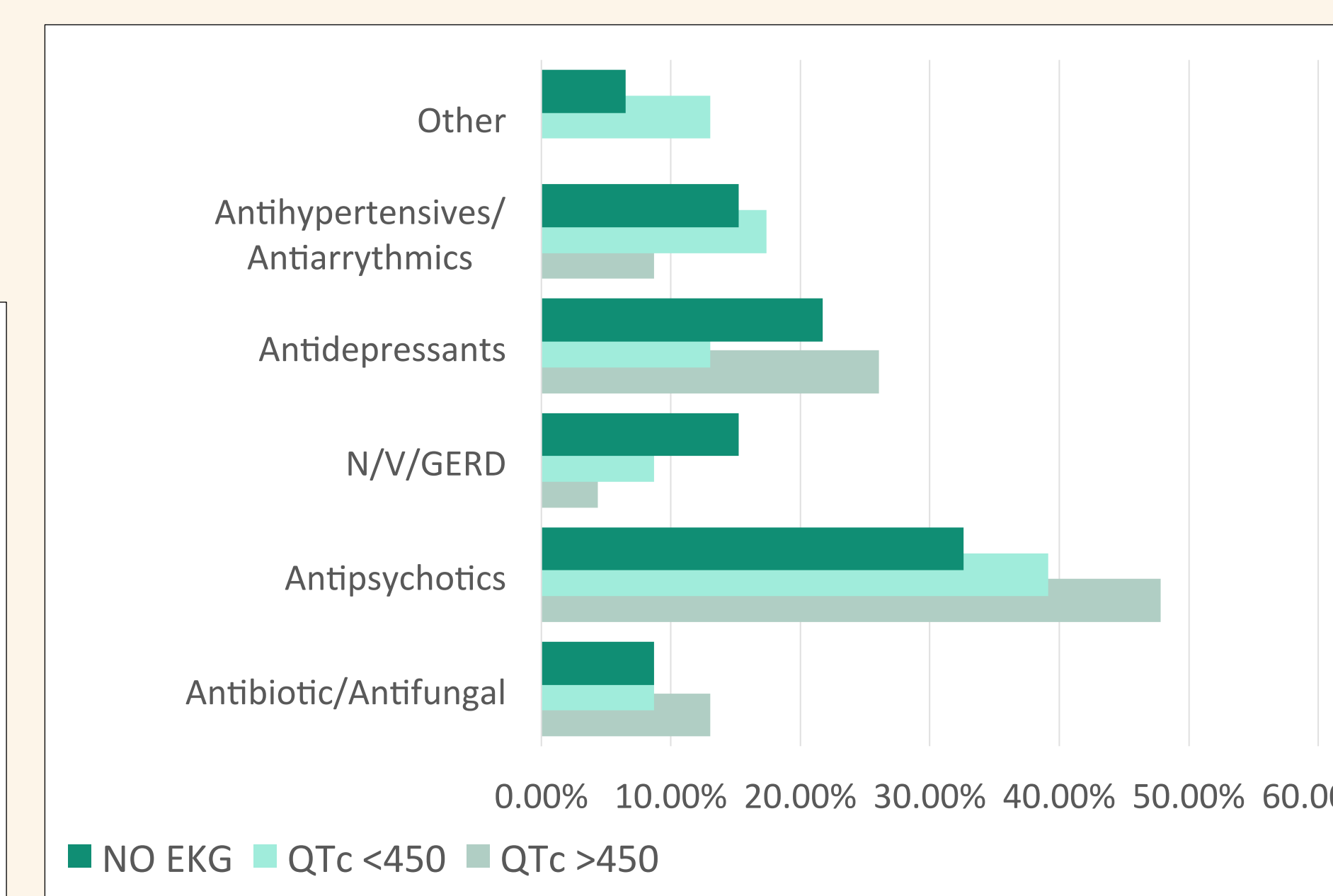


Figure 4. Distribution of Medication Class per Group. In general, patients who had elevated QTc intervals were on more antipsychotics and antidepressants compared to those with normal QTc intervals and with no EKGs. Patients with no EKG on file were on more antidepressants and gastrointestinal medications than those who had normal QTc intervals.

DISCUSSION

- For the 4/31 patients that met the initial inclusion criteria, the primary objective to determine the effect of pharmacist recommendations measured by a decrease in QTc interval was unable to be assessed due to lack of post-recommendation follow-up EKGs on file.
- The presence of coronary artery disease was found to be significantly higher in patients with elevated QTc intervals when compared between the three groups (p value = 0.07)(Table 1).
- Sub-analyses on 31 patients revealed that ~45% of patients at risk of QTc prolongation had no EKG on record and remained at risk (Figure 1). This provides an opportunity to develop a protocol under which pharmacists could order EKGs to monitor patients at risk.
- Though sub-analysis demonstrated no significant differences in the number of recommendations accepted, not accepted, and not made between the 3 groups, it is important to note that 55.6% of the patients with QTc ≥ 450 msec did not have a follow-up pharmacist recommendation (Figure 2).
- There was no significant difference in distribution of medications by risk category amongst groups, further emphasizing the need to monitor patients engaged in polypharmacy (Table 2).
- Evidence-based literature suggests that polypharmacy is becoming common practice in elderly and can increase the risk of drug-drug interactions, supporting the need for further assessment of additional risk factors. Careful EKG monitoring prior to and after administration of drugs with anticipated QTc prolongation may be warranted.

LIMITATIONS

- Small sample size limits generalizability
- Narrow demographic range: 100% Caucasian population
- Lack of EKG orders available, either upon admission, initiation of treatment, or follow-up
- Retrospective study: some amount of data may have been missing from medical records
- QTc interval as a surrogate measurement: QTc is rate-corrected and is reliable with normal T waves at physiological heart rates, but unreliable at elevated HR, abnormal T waves, and prominent U waves
- A multivariate linear regression analysis was not performed
- Potentially undetected hERG mutation: hERG mutation, a risk factor for QTc prolongation, was not completed
- Indication of medications did not always correlate to an ICD 9/10 diagnosis

CONCLUSION

EKGs are an easily accessible monitoring tool for QTc interval prolongation and are underutilized in the elderly population. The findings in this study suggest the consideration of a new protocol under which pharmacists can order EKGs for medication monitoring purposes to maximize patient safety. Though the American Society of Consultant Pharmacists reports that there has been a 27% reduction in antipsychotic use in nursing home residents and that the national prevalence of antipsychotic medication usage has fallen to 17.4% as of the third quarter of 2015, in general, polypharmacy is still on the rise. For this reason, the concern of multiple QTc prolonging medications leading to increased risk of TdP remains. Increased awareness of potential complications can allow pharmacists and physicians to better manage and monitor elderly patients at risk of polypharmacy-induced QTc prolongation.

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