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DRUG-DRUG INTERACTIONS WITH QT-PROLONGING DRUGS IN PATIENTS ADMITTED TO A CARDIOVASCULAR DEPARTMENT: A RETROSPECTIVE ANALYSIS

AIMS

- **characterize** QT-prolonging drug-drug interactions (QT-DDIs) identified in patients admitted to the Cardiovascular Department in the University Hospital
- **compare** significance ratings between our local DDI database and widely recognized Lexi-Interact DDI database

MATERIALS & METHODS

- a **retrospective analysis** of the electronic medication records with a built-in DDI database
- **study location: Cardiovascular Department (CD)** with 50 Standard and 12 ICU beds, University Hospital Ostrava, Czech Republic
- **study population:** pts with ≥1 **highly significant QT-prolonging DDI** (5 or 6 on 0-6 scale, very severe or contraindicated) within hospitalization, during the study period (January - December 2019)
- DDI database used in the hospital: DrugAgency Database (DrugAgency, Inc., Prague, Czech Republic)
- comparator DDI database: Lexi-Interact (Lexicomp Online, Hudson (OH), Lexicomp, Inc.)

RESULTS

stations	patients with ≥ 1 QT-DDI within hospitalization in Cardiovascular Department	total number of QT-DDIs in these patients
Standards	149/5341 (2.8 %)	193
ICUs	81/909 (8.9 %)	125
Total	**230/6250 (3.7 %)**	**318**

some patients experieced multiple QT-DDIs (more often in ICUs vs Standards)

QT-DDIs were more frequent in ICUs vs Standards

230 of 6250 pts (3.7 %) hospitalized in CD experienced ≥ 1 QT-prolonging DDI within hospitalization = STUDY POPULATION
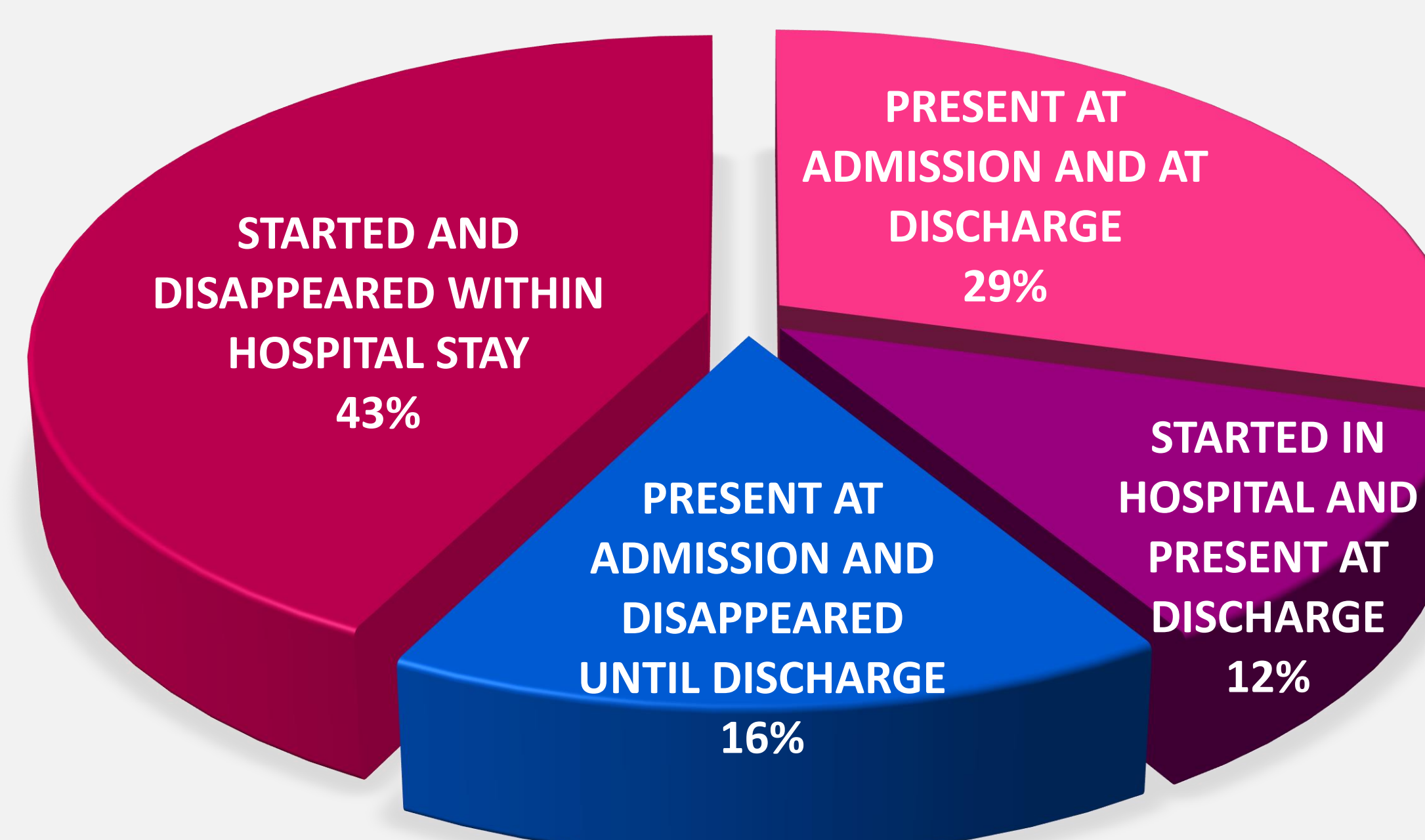
n = 230; M/F: 122/108
mean age (median; range): 74.5 years (77; 29 - 99)
mean No. of meds at admission (median; range): 11.5 (11; 2 - 23)

➤ 51 patients (22 %) has multiple QT-DDIs and
➤ 20 patients (9 %) has ≥ 3 QT-DDI in the medication
➤ 1 patient experienced 9 QT-DDIs that were a result of the 6-drug combination (ciprofloxacin, citalopram, clarithromycin, quetiapine, melperone, tramadol)
➤ 7 patients (3 %) experienced drug-associated long QT syndrome (1 of them didn't have any antiarrhythmics in the medication) – see table down right

TIME COURSE OF THE QT- DDIs

STARTED AND DISAPPEARED WITHIN HOSPITAL STAY 43%
PRESENT AT ADMISSION AND AT DISCHARGE 29%
STARTED IN HOSPITAL AND PRESENT AT DISCHARGE 12%
PRESENT AT ADMISSION AND DISAPPEARED UNTIL DISCHARGE 16%

MOST FREQUENT QT-DDIs

drug 1	drug 2	occurrences
melperone	tiapride	36
amiodarone	ciprofloxacin	34
amiodarone	tiapride	25
amiodarone	melperone	18
tramadol	sertraline	18
amiodarone	citalopram	14
amiodarone	clarithromycin	14
tramadol	melperone	14
amiodarone	escitalopram	10
tramadol	citalopram	10
TOTAL		**318**

tiapride, melperone – atypical antipsychotics

DIFFERENCES IN DDI SIGNIFICANCE RATING BETWEEN DATABASES

drug 1	drug 2	DAD (used in hospital)	LEXI-INTERACT
amiodarone/sotalol	venlafaxin	5	no DDI
amiodarone/sotalol	amantadine	5	no DDI
(es)citalopram	donepezil	5	B
clarithromycin	ciprofloxacin	5	B
clarithromycin	citalopram	5	C
ciprofloxacin	(es)citalopram	5	B

significance rating scales: DAD: 0-6; Lexi-Interact: A-D, X

PATIENTS THAT EXPERIENCED DRUG-ASSOCIATED LQTS

M/F (age)	QT-prolonging medications
F-86	donepezil, escitalopram (both chronic); kalemia – lower limit
M-88	amiodarone IV/PO (loading), ciprofloxacin IV, tiapride IV/PO, melperone PO at bedtime (all meds started in hospital), normokalemia
M-68	amiodarone PO, citalopram PO (both chronic); hypokalemia
F-57	amiodarone PO/IV (loading), tiapride PO/IV as needed, ciprofloxacin IV (both temporary), escitalopram (chronic); hypokalemia
M-69	amiodarone PO, citalopram, melperone PO at bedtime (all meds chronic); normokalemia
M-82	amiodarone PO (loading), clarithromycin IV, fluconazole IV/PO (both temporary); hypokalemia
F-66	amiodarone PO, escitalopram (both chronic) + levofloxacin IV (temporary); slight hypokalemia

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CONCLUSIONS

- QT-prolonging DDIs were common among CD inpatients. Single & multiple DDIs were more frequent among ICU than Standard patients.
- It is useful for safe and effective pharmacotherapy to monitor DDIs in the hospital - which DDIs are most common, how the physicians manage significant DDIs, how are they familiar with DDI tools.
  - Consult more DDI tools is reasonable. There may be substantial differences in DDI significance rating - seek specialist advice, if in doubt.
    - The role of clinical/hospital pharmacist as a consultant seems essential.

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