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Appropriateness evaluation of DOAC dosing, after implementation of algorithms designed to detect inappropriate dosing

Master Thesis - spring semester 2020

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ABSTRACT

BACKGROUND AND OBJECTIVES: In March 2019 at the tertiary care hospital in Aarau, several algorithms were implemented to detect inappropriate dosing of direct oral anticoagulants (DOACs). The dosage of the DOACs rivaroxaban, apixaban, edoxaban and dabigatran in terms of congruence of patient's age, weight, renal function and also indication with the prescribed DOAC dosage in a restricted form are checked by the algorithms. The main objective of this master thesis was to analyze the impact of the algorithm's implementation. Therefore, prevalence and risk for inappropriate dosing were determined. Risk factors for inappropriate dosing and the influence of possible reasons for underdosing (PRFU) on dosage appropriateness were explored. Further sensitivity, specificity and acceptance rates for interventions of the algorithms were calculated.

METHODS A retrospective cohort study was conducted on all inpatients with at least one DOAC intake between 01.03.-31.12.2018 (pre-implementation) and 01.03-31.12.2019 (postimplementation). Exclusion criteria were no informed consent, age < 18, DOAC intake > 24 h before discharge, missing data for determination of correct dosage (e.g. indication). Congruence of age, weight, renal function (CKD-EPI) and indication of patient's last DOAC prescription before discharge were examined. Appropriateness was judged by summary of product characteristics (SmPC). Risk factors for inappropriate dosing (and its subgroups contraindications, overdosing and underdosing) were determined to adjust the logistic regression for any confounders, in order to analyze the impact of the algorithms on dosage appropriateness at discharge overall and per DOAC. PFRU were: Antiplatet drug therapy, reduced eGFR calculated with Cockroft Gault Formula, and only one instead of two fulfilled criteria for dosage reduction in case of apixaban in atrial fibrillation (AF). The influence of PRFU on dosage appropriateness was explored by a second logistic regression additionally fitted for PRFU.

RESULTS: A total of 4635 cases were evaluated, 2701 were included (2018: 1287, 2019: 1414). Most patients received an anticoagulation for AF. Rivaroxaban was the most prescribed DOAC in both years but prescriptions decreased significantly in 2019, whereas apixaban use increased in 2019. While the prevalence and risk for any inappropriate dosing in 2019 were significantly reduced for edoxaban/dabigatran prescriptions (21.8% to 8.6%, p: 0.002 // OR 0.31, p: 0.002), significant reduction was not achieved over all DOACs, (19.3% to 17.0%, p: 0.12 // OR 0.86, p: 0.141). There was a significant reduction of prevalence and risk for the subgroup contraindications (2.7% to 0.4 %, $p < 0.001$ // OR: 0.15, $p < 0.001$) in 2019. Contrary, the prevalence and risk for underdosed apixaban prescriptions increased in 2019 (13.6% to 19.5%, p: 0.023 // OR: 1.54, p: 0.025). It is to say that PRFU significantly increased overall prescriptions in 2019 and apixaban cases showed a very high prevalence (> 76%) of PRFU. Prevalence and risk for overdosing were insignificantly reduced overall DOAC prescriptions in 2019 compared to 2018 (3.2% to 2.5%., p: 0.32 // OR: 0.77, p: 0.275). The prevalence and risk of overdosed Rivaroxaban prescriptions were significantly reduced. A sensitivity of 62% and a specificity of 92% overall algorithms were calculated. The overall acceptance rate of interventions was 88% for contraindication, 85% for overdosing and 47% for underdosing.

CONCLUSION: The algorithms had a positive impact on dosage appropriateness even if significance could not be shown for every DOAC and every kind of inappropriateness. It was assumed that the prevalence and risk of underdosed prescriptions increased from 2018 to 2019, due to significantly more apixaban prescriptions in 2019 with dual or triple anticoagulation as supported by the adjusting for PRFU. The algorithms showed a good specificity, but a lower sensitivity because diagnoses are not coded in our clinical information system (CIS). Therefore, especially underdosed cases are less identified. Another limitation was that algorithms alerts were not sent directly to the physician in order to avoid clinically not relevant alerts. The overall high acceptance rate shows that this is a good strategy to get the intervention accepted and the therapy optimized. So far, the algorithms run on an external software. By implementing them directly into the clinical physician order entry (CPOE), a further reduction of inappropriate dosing of DOAC by shortening the timespan between inappropriate prescription and detection is estimated.