

the combined occurrence of stroke, TIA, cardiovascular death and acute coronary syndrome (ACS). Furthermore, we collected data about clinical parameters (age, sex, ethnicity), co-medication during follow-up and vascular risk factors.

We tested the association between carrying LOF or GOF alleles and the primary endpoint in a univariate analysis, and multivariate analysis including those clinical parameters previously related to clopidogrel response. OR and HR were calculated and P-values <0.05 were considered statistically significant.

**Results** Sixty-seven patients were recruited, 53 (79.1%) because of stroke, mean age 68.2±9.83 years, 35.8% females and 100% caucasians. Carrying *CYP2C19* LOF alleles was significantly associated with the primary endpoint in the single analysis (OR=3.82; 95% CI: 1.1 to 13.2; p=0.028), in the multivariate analysis (OR=5.07; 95% CI: 1.2 to 21.45; p=0.023). This association remains significant if we perform a survival analysis (HR=3.01; 95% CI: 1.01 to 9.0; p=0.048). Carrying *CYP2C19* GOF alleles was not related to the primary endpoint in the univariate analysis but, in the multivariate analysis, it was significantly associated with a protection against the primary endpoint.

**Conclusion** *CYP2C19* LOF polymorphisms may be used as genetic markers of clopidogrel response in cerebrovascular disease patients. Among these patients, *CYP2C19* GOF allele may be considered as a protector against the primary endpoint.

#### REFERENCES AND/OR ACKNOWLEDGEMENTS

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No conflict of interest.

#### 5PSQ-010 MANIPULATION OF WARFARIN TABLETS IN PAEDIATRIC CARE: DO WE GIVE THE RIGHT DOSE?

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**Background** Manipulation of drug formulations to achieve an appropriate dose is often necessary in the paediatric ward (e.g crushing and dispersion of tablets, followed by extraction of a fraction). However, such manipulation has previously been shown to result in inaccurate dosing for some tablet formulations of the poorly soluble anticoagulant aspirin. Using the same manipulation procedure, a dispersible tablet formulation of aspirin yielded 99% of the intended dose while a chewable tablet yielded only 9%.<sup>1</sup> Warfarin is another anticoagulant used in paediatric care. Despite having good solubility, ensuring a reliable dose of this substance is important, considering the narrow therapeutic index of the drug.

**Purpose** To investigate the dose accuracy and dose precision attained after manipulation of two different warfarin tablets, using validated ultra high-performance liquid chromatography (UHPLC-analysis).

**Material and methods** Warfarin tablets: Marevan (2.5 mg; Takeda AS, Norway) and Warfarin Orion (2.5 mg; Orion Pharma, Finland). Instrument: UHPLC-system from Shimadzu Corp (Nexera, with Prominence DAD-detector). Analytical column: Inertsil 2 µm C8-3, 2.1 × 100 mm, (GL Sciences Inc., Tokyo, Japan). The analytical method was validated for linearity, precision and specificity. Dosing accuracy study: six tablets

from each of the two formulations were individually dissolved in 10 ml water. After 8 min, a sample (1 ml) was withdrawn. Dosing accuracy and precision was recorded and compared between formulations.

**Results** For Warfarin Orion (2.5 mg) 96.5% (SD 4.8; range 89.8%–101.4%) of the intended dose was found. For Marevan (2.5 mg) 101.4% (SD 4.2; range 96.3%–107.2%) of the intended dose was found.

**Conclusion** Using a validated UHPLC-method, the dosing accuracy upon dispersion and dose extraction from two warfarin tablets (Marevan and Warfarin Orion) was found to be both accurate and precise – unlike that which had previously been published for different aspirin tablets. These results underline the importance of considering both formulation and drug characteristics when manipulating tablets.

#### REFERENCES AND/OR ACKNOWLEDGEMENTS

1. Notaker N, Brustugun J, Tho I, Bjerknes K. Manipulation and formulation – the tale of two aspirin tablets. Poster abstract. EAHP 2016.

No conflict of interest.

#### 5PSQ-011 VENOUS THROMBOEMBOLIC EVENTS AND TOTAL HIP OR KNEE ARTHROPLASTY: INCIDENCE AND ASSOCIATED FACTORS

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**Background** Orthopaedic surgery is associated with a high risk of venous thromboembolism events (VTE), especially in total hip arthroplasty (THA) or total knee arthroplasty (TKA). The incidence of VTE with pharmacological prophylaxis after THA or TKA was 0.7%.<sup>1</sup> Although this incidence is low, these adverse events are serious and usually preventable.

**Purpose** The aims of this study were to evaluate the incidence of VTE and the factors associated with a VTE after THA or TKA.

**Material and methods** To evaluate this incidence in 2017, the numerator (number of stays with VTE after THA or TKA) and the denominator (number of stays of patients hospitalised to THA or TKA) were obtained from diagnosis related groups (DRG) data. Some demographic and medical characteristics of stays were extracted from DRG data. Information related to the thromboprophylaxis were obtained by analysing prescriptions of the whole stays. The factors associated with a VTE were identified according to Fisher's exact test.

**Results** A total of 833 stays of THA and TKA were identified. The patients' mean age was 72.2 years. The most common thromboprophylaxis was the use of low-molecular weight heparin (LMWH) in postoperative and rivaroxaban over the following days.

The incidence of VTE was 0.48%. The patients' mean age with VTE was 74 years. The most common thromboprophylaxis was the use of LMWH in postoperative and dabigatran. In the study, any factors were not significantly associated with VTE (p>0.05).

**Conclusion** In our study, the incidence was low. Our prescription software proposed protocols of thromboprophylaxis standardised according to patients' characteristics, especially age. The prescriptions were always performed by senior physicians. The thromboprophylaxis recommendations were respected. This study did not find characteristics significantly