

ASSESSMENT OF FUNCTIONAL OUTCOMES IN PATIENTS TREATED WITH KCENTRA® FOR THE REVERSAL OF BLEEDING SECONDARY TO WARFARIN OR DIRECT ORAL ANTICOAGULANTS IN THE SETTING OF AN INTRACEREBRAL HEMORRHAGE

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Disclosures

- No conflicts of interest to disclose

Learning Objective

- Compare functional outcomes between patients treated with prothrombin complex concentrate (PCC) for intracerebral hemorrhage (ICH) secondary to direct oral anticoagulant (DOAC) administration versus warfarin administration.

Research Question

- In adult patients presenting with intracerebral hemorrhage secondary to vitamin K antagonists or DOAC use did treatment with PCC lead to different functional outcomes between patient groups?

Background

- ICH is the second most common subtype of stroke and often leads to permanent disability
- Anticoagulant associated ICH
 - 0.3% – 0.6% per year for warfarin
 - 0.1% – 0.2% per year for DOACs
- PCC has demonstrated efficacy at reversal of both warfarin and DOACs in clinical trials

Joon An S, Jung Kim T, Yun B. *J Stroke*. 2017;1(19):3-10.
Steiner T, Weitz JI, Veltkamp R. *Stroke*. 2017;48(5):1432-1437.

Literature Review

	Song et al.	Erenberg et al.	Zheng	Piran et al.
Study Design	RCT	RCT	Retrospective observational	Meta-analysis
Purpose	PCC reversal of apixaban	PCC reversal of rivaroxaban	PCC reversal of DOAC-related bleeding	PCC reversal of DOAC-related bleeding
Outcome	ETP: + 425 nm /min (P < 0.001) No effect on anti-Xa	PTT reversal: 12.8 from 15.8 (P < 0.001) ETP reversal: 51 to 114 (P < 0.001)	Change in Hgb from baseline: - 3.22%	Effective bleeding control per ISTH criteria: 69% successful management (95% CI, 0.61-0.76)
Conclusion	PCC reverses the effects of apixaban	PCC reverses the effects of rivaroxaban	PCC may be effective at reversing DOAC-related bleeding	PCC effective at reversing DOAC-related bleeding

RCT = Randomized controlled trial

ETP = Endogenous thrombin potential

PTT = Partial thromboplastin time

Hgb = Hemoglobin

ISTH: International Society of Thrombosis and Haemostasis

Song Y, Wang Z, Perlstein I, et al. *Journal of Thrombosis and Haemostasis*. 2017;15(11):2125-2137.

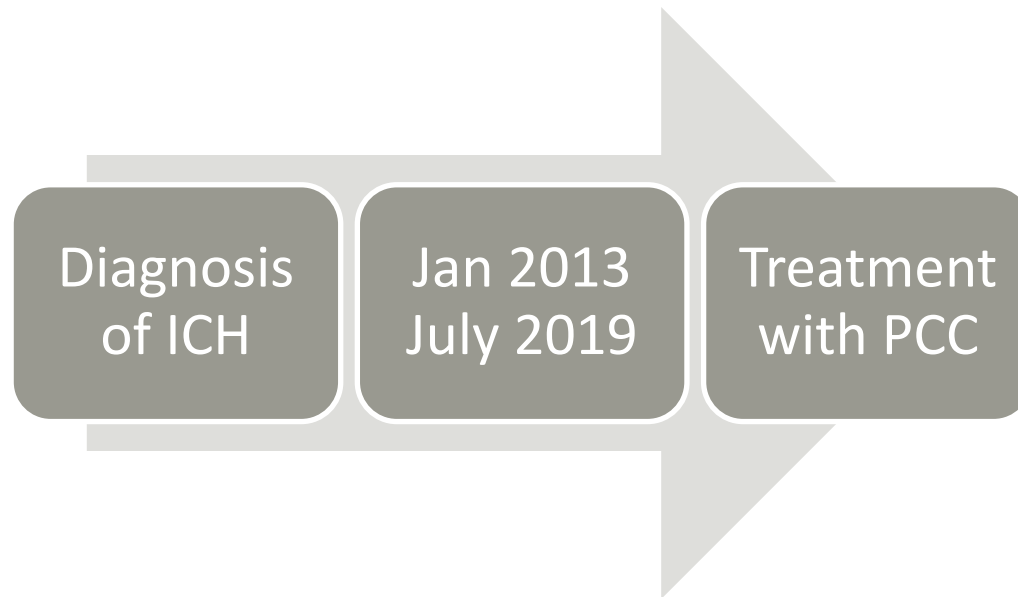
Erenberg ES, Kamphuisen PW, Sijpkens MK, et al. *Circulation*. 2011.

Zheng Y, Tormey C. *Blood*. 2017;130.

Piran S, Khatib R, Schulman S, Majeed A, Holbrook A. *Blood Adv*. 2019;3(2):158-167.

Study Design

- Retrospective, non-randomized, cohort review of patient electronic medical records from a community hospital.



Treatment Cohorts

- Patients treated with PCC for reversal of ICH due to warfarin.
- Patients treated with PCC for reversal of ICH due to DOAC.

Inclusion & Exclusion Criteria

Inclusion	Exclusion
<ul style="list-style-type: none">• Diagnosis of ICH admitted to SSM DePaul Hospital between January 2013 – July 2019• Treatment with warfarin or DOAC• Received PCC for reversal of bleeding	<ul style="list-style-type: none">• Death within 24 hours of PCC administration• Modified Rankin Score of 6 within 24 hours of PCC administration

Study Outcomes

- **Primary**: Change in Modified Rankin Score from admission until discharge
- **Secondary**:
 - Disposition at discharge
 - Mortality rate during hospital admission

Modified Rankin Score

Score	Definition
0	No symptoms
1	No significant disability. Able to carry out all usual activities, despite some symptoms
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities
3	Moderate disability. Requires some help, but able to walk unassisted
4	Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted
5	Severe disability. Requires constant nursing care attention, bedridden, incontinent
6	Death

Statistical Analysis

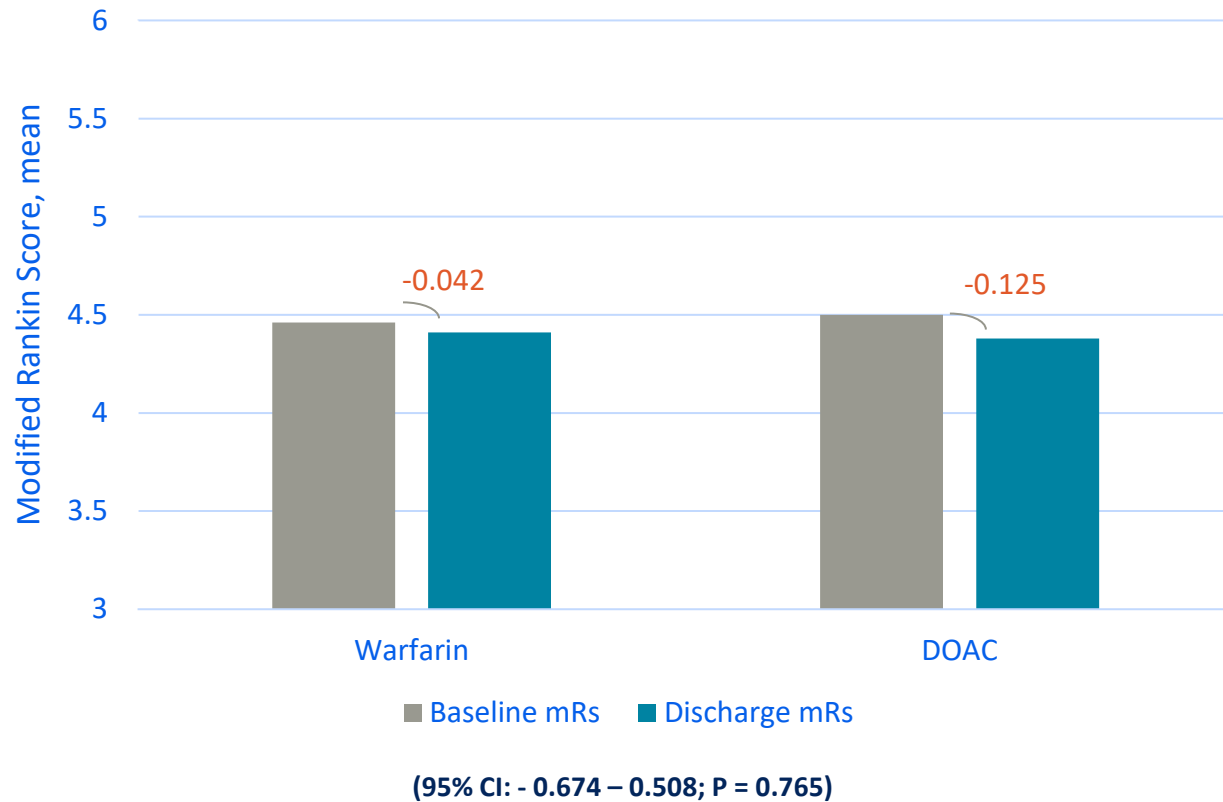
- Data analysis was completed using MiniTab® v.19 statistical software
- Baseline demographics were reported using descriptive statistics
- Primary outcome was analyzed using Student's T-test
- Secondary outcomes were analyzed using Chi-Squared test

Baseline Characteristics

Table 1. Baseline Patient Demographics			
	Warfarin (n = 40)	DOAC (n = 14)	P-value
Age	75.7	75.1	0.860
Gender	--	--	0.201
Male	25 (63%)	6 (43%)	--
Female	15 (37%)	8 (57%)	--
Weight (kg)	85.3	83.2	0.785
BMI (kg/m²)	29.51	28.57	0.714
Baseline hemoglobin (g/dL)	12.46	12.34	0.881
Baseline hematocrit (%)	37.50	37.16	0.876
Baseline GCS	11.53	12.43	0.417
Baseline NIH Score	12.8	15.45	0.473
Baseline Modified Rankin Score	4.46	4.50	0.844
Presence of traumatic brain injury	10 (25%)	2 (14%)	0.407

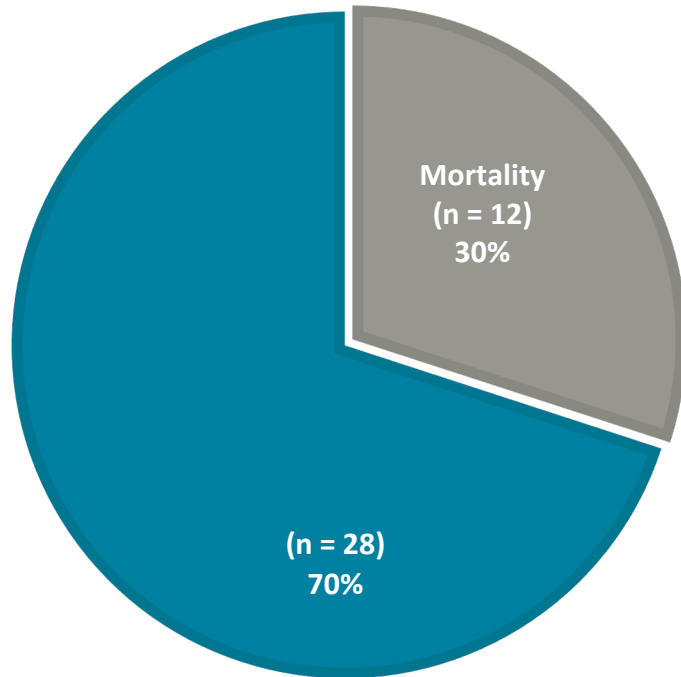
Primary Outcome:

Change in Modified Rankin Score

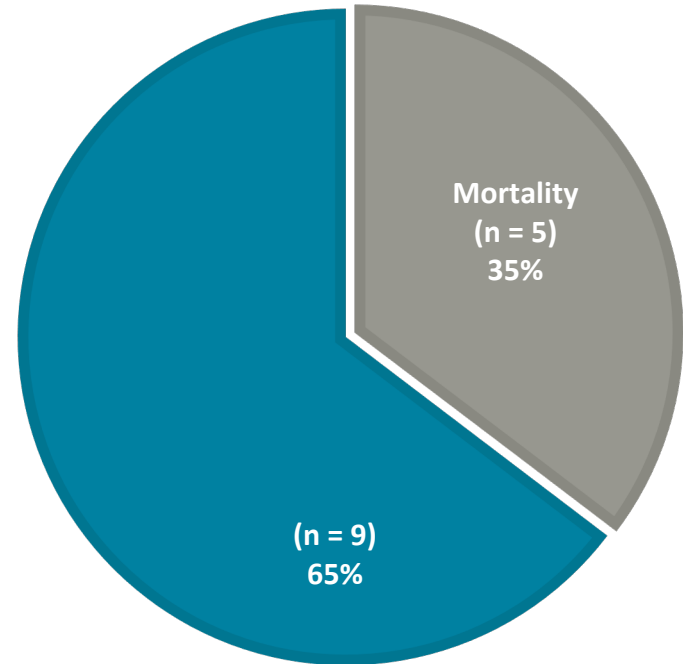


Secondary Outcome: Mortality

WARFARIN

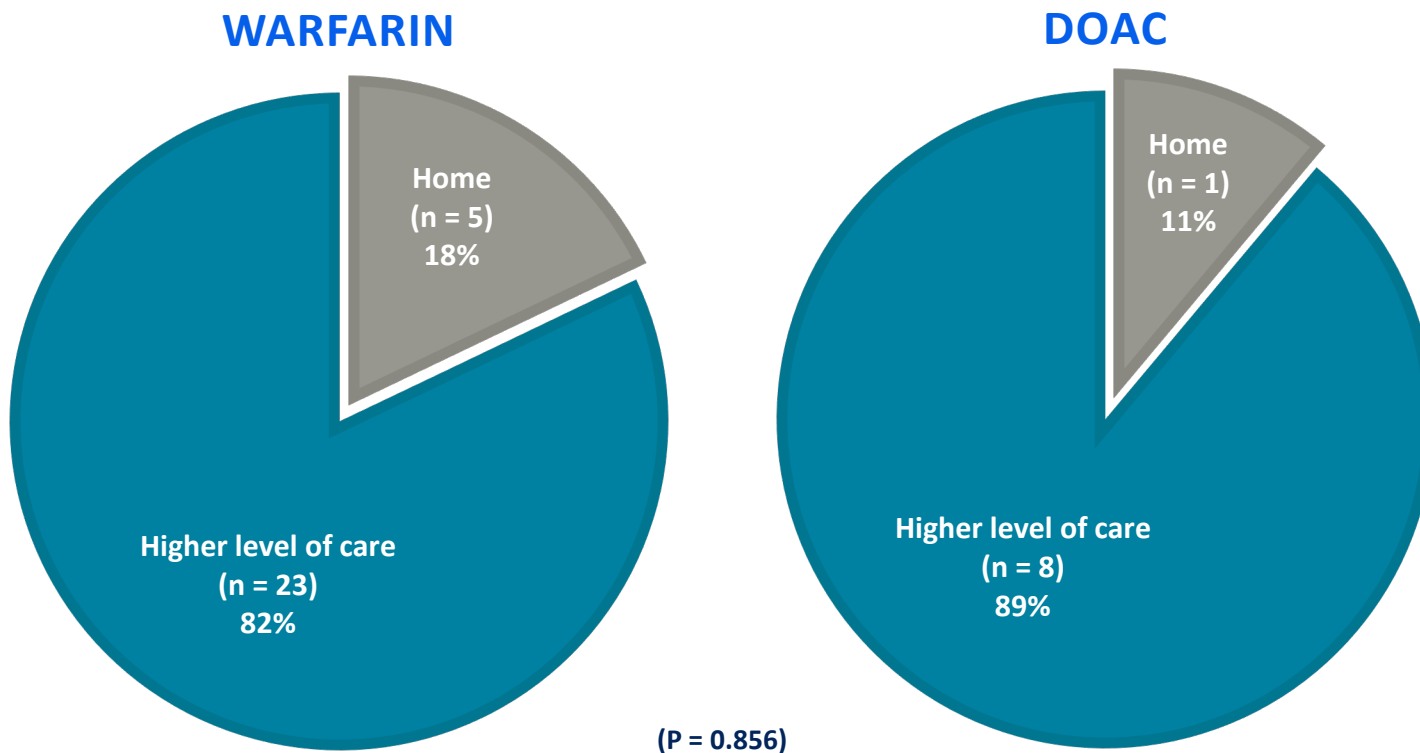


DOAC



(P = 0.692)

Secondary Outcome: Disposition at Discharge



Study Results

Table 2. Study Results			
	Warfarin (n = 40)	DOAC (n = 14)	P-value
Change in Modified Rankin Score	-0.042	-0.125	0.765
Mortality	12 (30%)	5 (35%)	0.692
Disposition at discharge	--	--	0.856
Facility/Higher level of care	23 (82%)	8 (89%)	--
Home/Home health	5 (18%)	1 (11%)	--
Hospital length of stay (days)	7.13	9.50	0.151
Post-PCC hemoglobin (g/dL)	11.51	12.33	0.317
Post-PCC hematocrit (%)	34.63	37.29	0.257
Change in NIH Score	2.63	4.86	0.425
ICU admission	18 (45%)	9 (64%)	0.214
ICU Length of stay (days)	2.45	4.36	0.154
Neurologic intervention required	7 (17.5%)	1 (7%)	0.348
Days of active sedation	1.13	0.93	0.703

Strengths & Limitations

Strengths	Limitations
<ul style="list-style-type: none">• Use of validated scales and scoring systems to assess functional outcomes• One of the first studies to evaluate functional status post PCC bleeding reversal for ICH	<ul style="list-style-type: none">• Small patient population• Single center study• Did not account for risk-enhancing conditions• Warfarin dose of patients not captured

Study Overview/Conclusion

- In this retrospective review of patients treated with PCC for the reversal of ICH due to warfarin or DOAC administration, there was no difference in functional outcomes found between treatment arms

Future Directions

- Larger trials are warranted to provide further data on functional patient outcomes in the setting of ICH following PCC administration
- Comparison of the relative cost-benefit profile of anticoagulation reversal with PCC for DOAC-induced ICH compared to newer and more expensive options

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