NOAC's

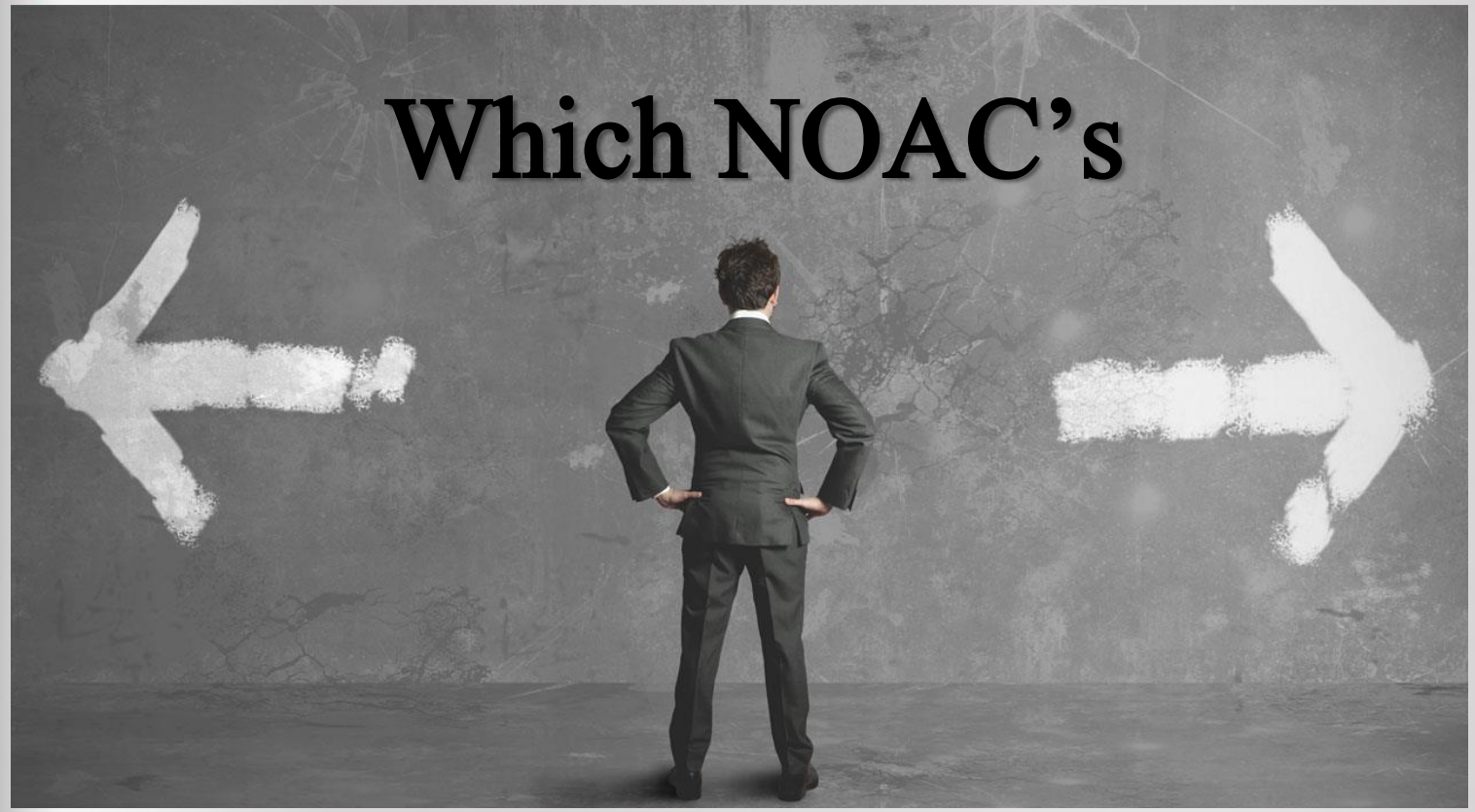
in Specific Population with NVAF

Clinical Case Scenarios

Interactive Presentation

JSECC Conference 2018 **Dr. Koren Ofir**

Which NOAC's



Meryl S. 78y

- HTN, DM-II, Diabetic Nephropathy
- Newly Diagnosed AF

Important Data	Medications	Bleeding History	Thrombotic Risk
• Weight • Creatinine Clearance • Liver Function • Drinking Habits • Frailty	1. Tritace 2.5mg 2. Multaq 400mg bid 3. Jardiance 10mg qd 4. Aspirin 75mg qd	Previous Major GI bleeding d/t Polyp	CHA_2DS_2-VASc

$CHADS_2$ criteria	Score
CHF/HFrEF	1
Hypertension	1
Age ≥75y	1
Diabetes melli	
Stroke/TIA/TE	2

CHA_2DS_2-VASc criteria	Score
CHF/HFrEF	1
Hypertension	1
Age ≥75y	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (prior MI, PVD or Aortic plaque)	1
Age 65–74y	1
Sex **c**ategory (female gender – added to other criteria)	1

CHA_2DS_2-VASc =5 (6.7%)

סל הבריאות \ רישום תרופה

המלצות קליניות
שיקול קליני

HAS-BLED SCORE	Score
Hypertension (>160 mmHg)	1
Abnormal Liver or Renal Function Renal – S. Creatinine >2.6 mg/dl, HD, Kidney Transplant Liver Cirrhoses, Bilirubin >x2, LFT >x3	1 1
Stroke	1
Bleeding – prior Major Bleeding, Predisposition (IDA, Polyps, Hemorrhoids)	1
Labile INR or TTR<60%	1
Elderly >65y	1
Drugs - Antiplatelets drugs and NSAIDs	1
Excess alcohol (≥8 drinks/week)	1

HAS-BLED=3 (5.8%)

Choose the Suitable Anti-Coagulation

Choose the Suitable NOAC

Why Not Coumadin ?

SAMe-TT2R2

Sex (female)	1
Age (<60 years)	1
Medical history (two of the following: hypertension, diabetes, MI, PAD, congestive heart failure, history of stroke, pulmonary disease, hepatic or renal disease)	1
Treatment (interacting medications e.g. amiodarone)	1
Tobacco use (within 2 years)	2
Race (non-Caucasian)	2

Score result	Action (Untested)[9]
0-2	Patients are likely to achieve a high TTR (e.g. >65%) so initiating with a VKA is likely beneficial.
≥3	Improve education regarding anticoagulation control (e.g. a structured educational programme[10]) or select a NOAC would be better initial options.

Elderly (≥75Yy)

Trial	Age ≥75	Results
RE-LY	7,258	More Bleedings in Elderly Patients
ROCKET-AF	6,229	Consistent results
ARISTOTLE	5,678	Consistent results

Contents lists available at SciVerse ScienceDirect

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New oral anticoagulants in elderly patients

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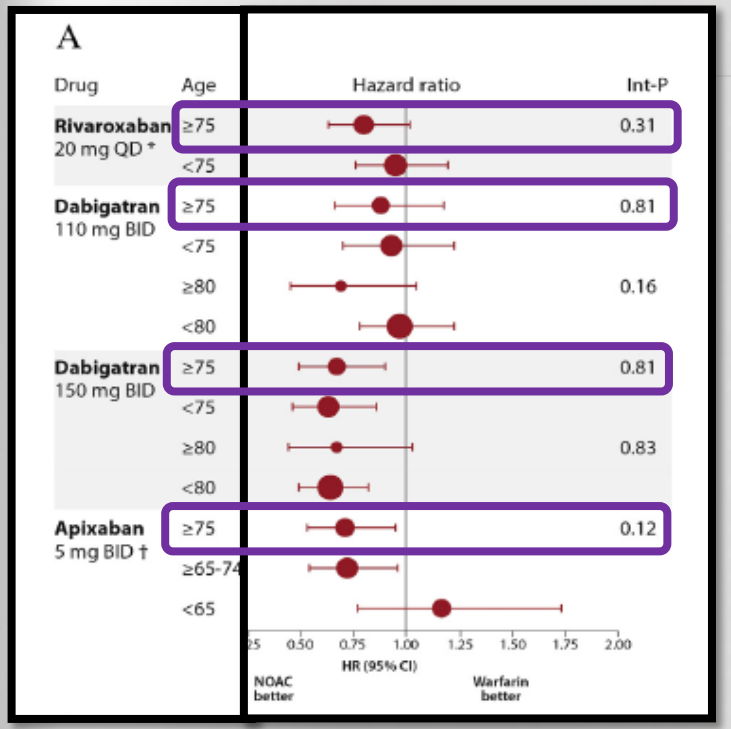
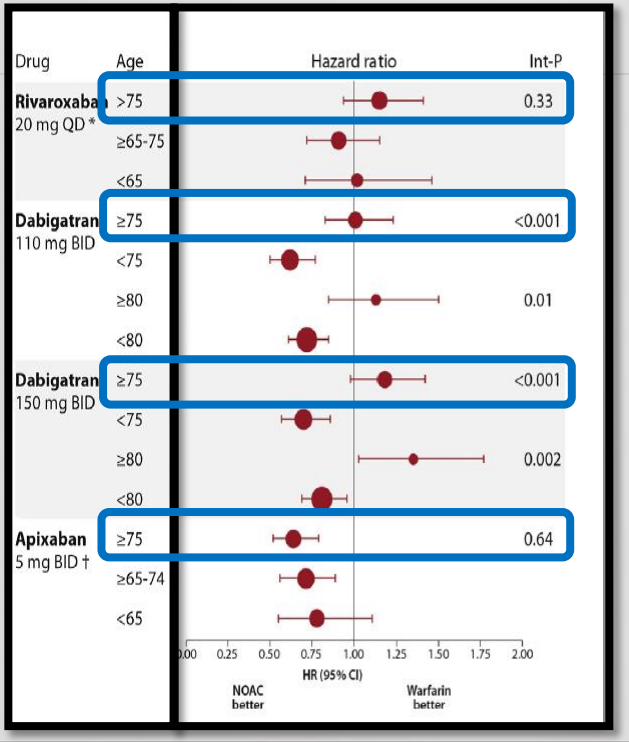
Stroke / SE

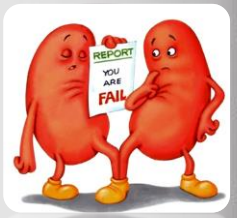


Major Bleeding



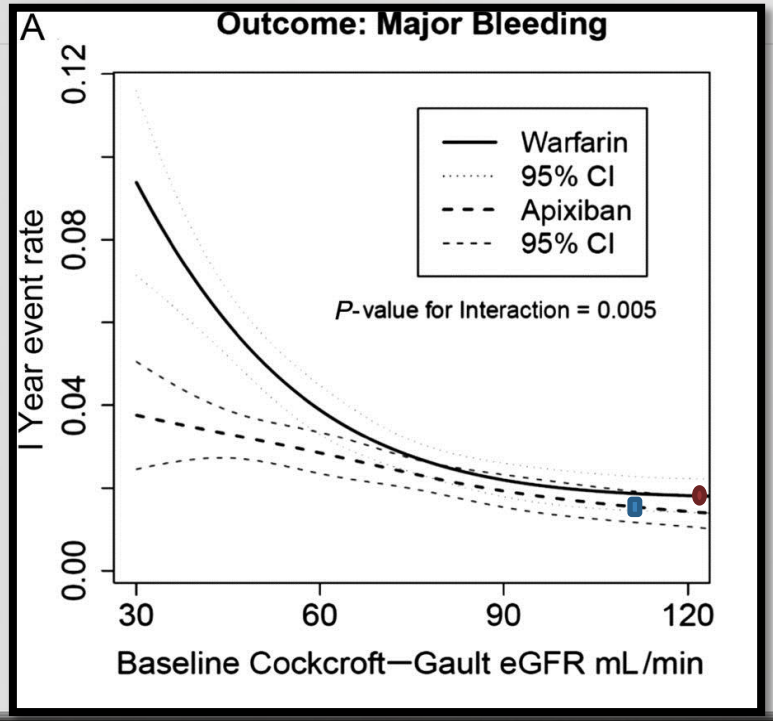
Elderly ≥ 75 y

- **NO Interaction** of Age and Safety or Efficacy
- Older patients had more bleeding but the overall pattern of bleeding observed showed **NO Difference**
- There was a Significant interaction between age and increased **Extra-Cranial Major Bleeding** with both doses of **Dabigatran**



Chronic Renal Failure (CKD)

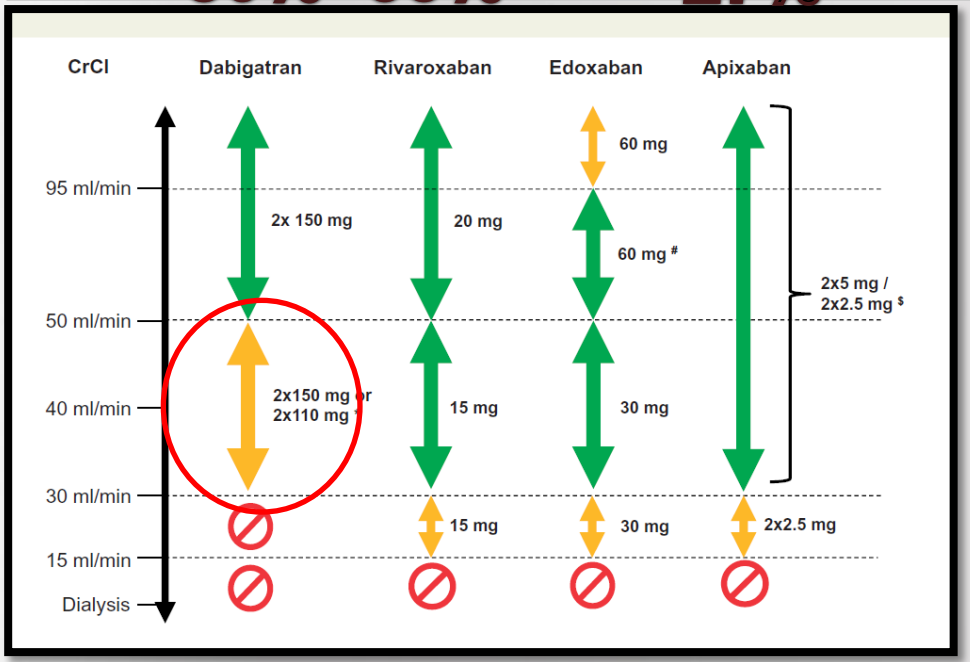
Major Bleeding in Relation to Renal Function



Hohnloser, SH et al.
Eur Heart J. 2012
Nov;33(22):2821-30

NOAC's According to Renal Function

80% 35% 27%



Efficacy of apixaban when compared with warfarin in relation to renal function in patients with atrial fibrillation: insights from the ARISTOTLE trial

Stefan H. Hohnloser[1]*, Ziad Hijazi[2,3], Laine Thomas[4], John H. Alexander[4], John Amerena[5], Michael Hanna[6], Matyas Keltai[7], Fernando Lanas[8], Renato D. Lopes[4], Jose Lopez-Sendon[9], Christopher B. Granger[4], and Lars Wallentin[2]

Oral anticoagulant therapy in patients with mild or moderate CKD (CrCl ≥30 mL/min)

trials.[190,195–199] In addition, the ARISTOTLE trial data analysis suggests that the bleeding benefit with apixaban compared with warfarin becomes significantly more prominent at lower CrCl values, while the stroke reduction benefit is maintained.[181,197] In contrast, the

Hohnloser, SH et al. Eur Heart J. 2012 Nov;33(22):2821-30

NOAC in Liver Disease

Parameters	1 point	2 points	3 points
Encephalopathy	No	Grade 1–2 (suppressed with medication)	Grade 3–4 (refractory/chronic)
Ascites	No	Mild (diuretic-responsive)	Moderate–severe (diuretic-refractory)
Bilirubin	<2 mg/dL	2–3 mg/dL	>3 mg/dL
	<34 µmol/L	34–50 µmol/L	>50 µmol/L
Albumin	>3.5 g/dL	2.8–3.5 g/dL	<2.8 g/dL
	>35 g/L	28–35 g/L	<28 g/dL
INR	<1.7	1.71–2.30	>2.30

Child–Pugh category	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
A (5–6 points)	No dose reduction	No dose reduction	No dose reduction	No dose reduction
B (7–9 points)	Use with caution	Use cautiously	Use cautiously	Do not use
C (10–15 points)	Do not use	Do not use	Do not use	Do not use

NOAC in High GI Bleeding

Recommendations	Class[a]	Level[b]
In patients at high-risk of gastrointestinal bleeding, a VKA or another NOAC preparation should be preferred over dabigatran 150 mg twice daily, rivaroxaban 20 mg once daily, or edoxaban 60 mg once daily.	**IIa**	**B**
Advice and treatment to avoid alcohol excess should be considered in all AF patients considered for OAC.	**IIa**	**C**

Kirchhof et al. *Eur Heart J.* 2016. doi:10.1093/eurheartj/ehw210.

Patient post major gastrointestinal bleeding

Continuing / Restarting NOAC?
Consider factors favouring withholding (✓) vs. (re-) starting anticoagulation

- ✓ Unidentifiable site of bleeding
- ✓ Multiple angiodysplasias in the G
- ✓ No reversable / treatable cause?
- ✓ Bleeding during treatment inter
- ✓ Chronic alcohol abuse
- ✓ Need for dual antiplatelet therapy after PCI
- ✓ Older age

Net assessment in favour of withholding anticoagulation according to a multidisciplinary decision

Yes

Consider no anticoagulation vs. LAA occlusion#

No

(Re-) initiate (N)OAC as early as feasible (after 4-7 days)
If >75 years old, consider NOAC other than dabigatran, rivaroxaban or higher-dose edoxaban as the first choice

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Frailty

CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Clinical Outcomes and History of Fall in Patients with Atrial Fibrillation Treated with Oral Anticoagulation: Insights From the ARISTOTLE Trial

Meena P. Rao, MD, MPH,[a] Dragos Vinereanu, MD, PhD,[b] Daniel M. Wojdyla, MS,[c] John H. Alexander, MD, MHS,[c] Dan Atar, MD, PhD,[d] Elaine M. Hylek, MD, MPH,[e] Michael Hanna, MD,[f] Lars Wallentin, MD, PhD,[g] Renato D. Lopes, MD, PhD, MHS,[c] Bernard J. Gersh, MB, ChB, DPhil,[h] Christopher B. Granger, MD[c] on behalf of the Apixaban for Reduction in Stroke Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) Investigators

Frailty

Event	Fall(s) Within 1 Year		
	Apixaban (n = 386)	W	
	Rate (Events)	Ra	
Stroke or SE	1.76 (12)	1	
Major bleeding	4.35 (26)	5	
Major or CRNM bleeding	8.81 (50)	9.15 (51)	0.95 (0.65-1.41)
Any bleeding	28.86 (135)	45.72 (181)	0.65 (0.52-0.81)
Hemorrhagic stroke	0.14 (1)	0.45 (3)	0.32 (0.03-3.09)
Intracranial bleeding	0.33 (2)	1.69 (10)	0.19 (0.04-0.88)
Subdural bleeding	0.00 (0)	0.85 (5)	–
Cardiovascular death	3.42 (24)	2.40 (16)	1.43 (0.76-2.70)
All-cause death	6.41 (45)	6.74 (45)	0.96 (0.63-1.44)
Stroke/SE/Major bleeding	5.82 (38)	6.79 (43)	0.85 (0.55-1.32)
Stroke/SE/Major Bleeding/Death	11.41 (75)	11.98 (76)	0.95 (0.69-1.31)

CI = confidence interval; CRNM = clinically relevant non-major; HR = hazard ratio; SE = systemic embolism.

CLINICAL SIGNIFICANCE

- Benefits of apixaban over warfarin were preserved, with an 80% reduction in intracranial bleeding; thus, apixaban appears to be a better alternative than warfarin for anticoagulation in patients with a history of falling.

Frailty

In summary, frailty *per se* should not be an exclusion criterion to anticoagulate since frail and older patients are at an increased risk of stroke and have been shown to benefit from OAC. The benefit of NOACs over VKA has best been demonstrated for edoxaban and apixaban in this patient population. To improve things further, all

Preferred

Second Choice

Avoid

Population	Eliquis 2.5\2.5mg	Xarelto 15\20mg	Pradaxa 110mg	Pradaxa 150mg
CKD IV	2.5mg	15mg	Second Choice	Avoid
LIVER DISEASE (Child-B)	5mg*	Avoid	110mg*	150mg*
Elderly (≥75)	5mg	Second Choice	Second Choice	Avoid
GI Bleeding	5mg	Avoid in Elderly	110mg	Avoid
Frailty	5mg	No Sufficient Data	No Sufficient Data	No Sufficient Data
Anti-Arrhythmic Agents (Ikavcor, Multaq)	5mg	5mg	MULTAQ / IKACOR	Avoid
ACS/PCI/Stenting	No Sufficient Data	20mg	110mg*	150mg*