



Bugs and Blood Drugs: ESRD Edition- Bloodstream Infections and Anticoagulation in Hemodialysis Patients

Wynnie Lau

BScPharm, ACPR, PharmD

Clinical Pharmacy Specialist, Nephrology St. Paul's Hospital

Nov 2020

CSHP BC Branch AGM

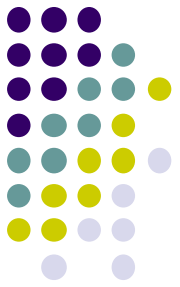
wlau@providencehealth.bc.ca

Disclosures



- Presenter's name: Wynnie Lau
- I have no current or past relationships with commercial entities
- I have received a speaker's fee from CSHP BC for this learning activity

Commercial support disclosure



- This program has received no financial or in-kind support from any commercial or other organization

Objectives



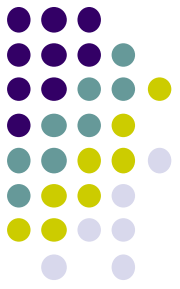
- By the end of this session the learner will be able to:
 - Provide evidence based recommendations with respect to antibiotic dosing in hemodialysis patients
 - Locate and utilize the blood stream infection algorithm located on the British Columbia Provincial Renal Agency (BCPRA) website
 - Describe the benefits/risks of warfarin use for ischemic stroke prevention in hemodialysis patients with atrial fibrillation
 - Describe the currently available studies on apixaban use in hemodialysis patients with atrial fibrillation

Case of MS



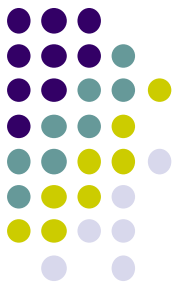
- CC: Fever and SOB
- HPI: MS 82yo male, 2wks of feeling fatigue and ↑ pain near his HD catheter site. Feeling febrile this morning and now in ER for assessment
- Past medical history
 - End stage renal disease (ESRD)
 - chronic hemodialysis (HD) for 3yrs
 - Hypertension (HTN)
 - Type 2 Diabetes Mellitus (T2DM)
 - Cerebrovascular accident (CVA) 6 months ago

Case of MS



- Physical exam
 - Temp 39° BP 185/90, HR 100, RR 25, O₂ sats 100%
 - Right subclavian hemodialysis catheter
 - erythema and pus is visible from surface
 - Irregular pulse
 - Current weight 90kg with pedal edema +2
 - Goal weight 86kg on hemodialysis prescription
- Labs:
 - WBC 15; Hgb 85; Plt 250
 - A1C 6.5 (1 month ago)
- Diagnostics
 - ECG: Atrial fibrillation
 - Holter done 1 month ago also shows Afib

Case of MS



- Allergies: NKDA
- Medications:

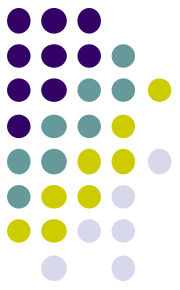
Anemia	Epoetin 4000 units IV qweekly (on Thursdays)
	Sodium ferric gluconate 125mg IV qmonthly (received 2 wks ago)
HTN	Amlodipine 10mg daily
T2DM	Insulin glargine 10 units qHS
CVA 2° prevention	ASA 81mg po daily
	Simvastatin 40mg po daily
Urine Output	Furosemide 120mg po daily

Medical Problem List

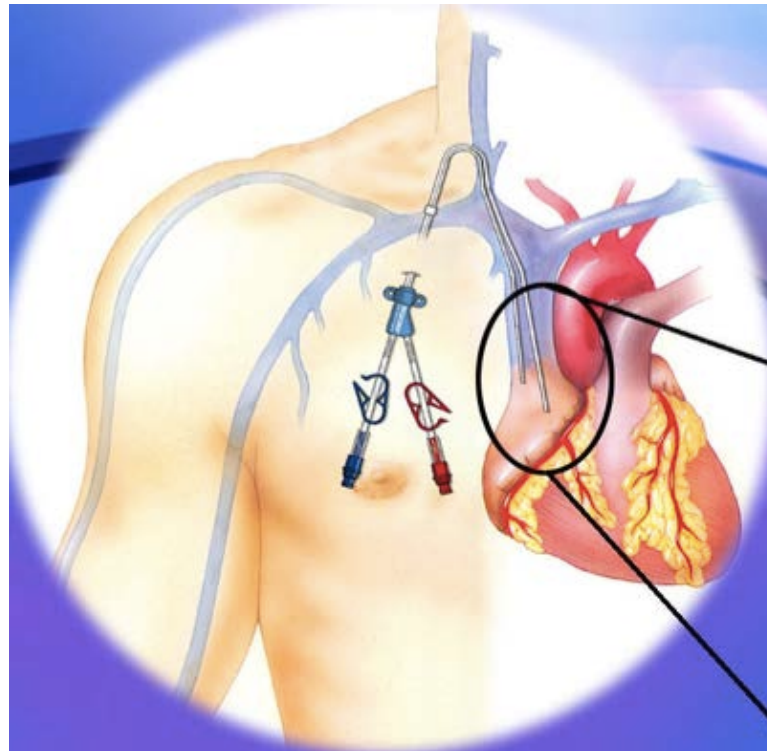


- Catheter Infection
- New? Atrial Fibrillation
- Hypertension
- Anemia

Hemodialysis catheter infection



- HD catheter infection mortality rates are 12- 25%
- Risk of bacteremia increases linearly with duration of HD catheter use



Catheter infection

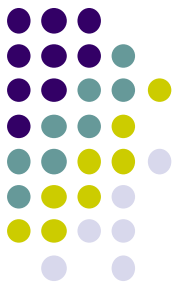


Table 6 Incidence of bacteremia in haemodialysis patients using permanent catheters by pathogenic species in a national prospective Canadian study and Quebec surveillance programme

Organism	Incidence ^a (%)	SPIN-HD Incidence ^b (%)
<i>Staphylococcus aureus</i>		
<i>Coagulase negative staphylococci</i>		
<i>Enterococcus spp.</i>		
<i>Streptococcus spp.</i>		
<i>Enterobacter spp.</i>		
<i>Pseudomonas spp.</i>		
<i>Candida spp.</i>		
<i>Klebsiella spp.</i>		
<i>Corynebacterium spp.</i>		
<i>Escherichia coli</i>		
<i>Stenotrophomonas maltophilia</i>		
<i>Other spp.</i>		
Incidence rate (per 1000 patient-procedures)		

^aAdapted from Taylor et al, 2002

^bAdapted from 2014 to 2015 SPIN-HD surveillance data [36]

^cIncludes grouped enteric and anaerobic organisms

Back to MS



- Gram stain of HD catheter culture:
 - +3 Polymorphonuclear cells
 - +3 Gram positive cocci
- Blood culture: Pending

- Vancomycin 25mg/kg IV x1 STAT started
 - Use patient goal weight

Catheter related infection



- When dosing antibiotics, consider drug removal by:
 - Residual renal function
 - Hemodialysis removal
 - Duration of hemodialysis:
 - 3hrs of HD, Vancomycin drug removal: $30\% \pm 7\%$
 - 4hrs of HD, Vancomycin drug removal: $38\% \pm 8\%$
 - Size of dialyzer filter
 - FX600 vs FX1000



BCPRA bacteremia treatment algorithm

Table 1: Treatment of Catheter-Related Bloodstream Infection- Page 2 of 2 (Algorithm)

- Clinical signs & symptoms
- Temperature remains elevated
- Recent catheter-related

Staphylococcus aureus

Catheter & Locking Solution:

- Remove catheter and replace at new site¹

Systemic Antibiotics:

- For methicillin-resistant (MRSA) or severe beta-lactam allergy², vancomycin:
 - Loading dose: 25 mg/kg IV
 - Maintenance dose: 500 mg if <70 kg or 750 mg if ≥70 kg administered post HD
 - Monitor level pre-HD & adjust to target 15 – 20 mg/L
- For methicillin-sensitive (MSSA):
 - Inpatient: cloxacillin 2g IV q4h post-HD
 - Outpatient: ceFAZolin 2g IV post HD

Treatment duration:

- Uncomplicated (resolution of fever and bacteremia within 72 hrs and no intravascular hardware): Treat 3 weeks from first negative blood culture
- Complicated (prolonged fever, bacteremia or septic thrombosis): Treat 4 weeks from first negative blood culture
- Metastatic complication (osteomyelitis, endocarditis): Treat 6 – 8 weeks from first negative blood culture. Consider ID consult

Treatment duration:

- Uncomplicated (resolution of fever and bacteremia within 72 hrs and no intravascular hardware): Treat 3 weeks from first negative blood culture
- Complicated (prolonged fever, bacteremia or septic thrombosis): Treat 4 weeks from first negative blood culture
- Metastatic complication (osteomyelitis, endocarditis): Treat 6 – 8 weeks from first negative blood culture. Consider ID consult

indications
: valve

erria

olution:

- negative for all above parameters: and use antibiotic lock solution post HD x 3 final concentrations):
mg/mL + heparin 2500 units/mL (if
- lactam allergy²: gentamicin 1 mg/mL + units/mL
- positive for any above parameter: and replace at new site¹
- post HD am allergy²:
500 – 750 mg PO or 400 mg IV q24h; OR
- se: 2 mg/kg IV
ice dose: 1.5 mg/kg IV post-HD
vel pre-HD and adjust to target <3.5 mg/L
- d/replaced, treat with antibiotics for 2 ative blood culture. Extend to 3 weeks if ved/replaced
- s not recommended as the sole antibiotic tiamase producing organisms (Serratia, tobacter, Morganella, Citrobacter, Proteus rogenes and Enterobacter) or extended mase (ESBL) producing organisms. If any of present, consider using appropriate eropenem or piperacillin-tazobactam

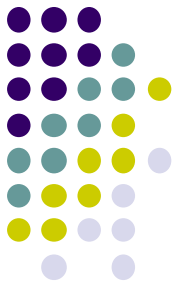
Note: If the culture is positive for a fun Draw repeat cultures 1 week after con

¹ Creating a new tunnel in the same sit
² ceFAZolin, ceftriaxone and ceftAZIDir symptoms, Stevens-Johnson syndrom

for at least 2 weeks following line removal.

reaction with eosinophilia and systemic

Treatment: *E. Faecalis* bacteremia



Systemic Antibiotics:

- **Vancomycin:**
 - Loading dose: 25 mg/kg IV
 - Maintenance dose: 500 mg if <70 kg or 750 mg if \geq 70 kg administered post HD
 - Monitor level pre-HD & adjust to target 15 – 20 mg/L

Inpatients:

- Ampicillin 2 g IV q12h (post-HD on HD days)

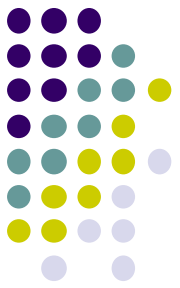
Treatment duration:

- Treat 2 weeks from first negative blood culture
- If endocarditis is present or suspected:
 - Extend treatment to 6 weeks
 - For synergy, may add ceftriaxone 2g IV q12 h for 6 weeks. If severe beta-lactam allergy², use gentamicin 1 mg/kg IV post HD x 2 wks. Adjust to maintain trough <2 mg/L

If VRE is isolated, give daptomycin 8 – 10 mg/kg IV qHD (3x/wk minimum) or linezolid 600 PO/IV BID. Consult ID

Note: Past VRE-positive swab does not predict that Enterococcus isolated will be VRE

Vancomycin Resistant Enterococcus (VRE) Bacteremia – Daptomycin dose



- If VRE is isolated, give daptomycin 8 – 10 mg/kg IV qHD (3x/wk minimum) or linezolid 600 PO/IV BID. Consult ID
- Diolez J et al AJKD 2017;70(5):732-4
 - n=11 HD patients with gram positive bacteremia and existing device (CVC or vascular or orthopedic prosthesis)
 - Daptomycin median dose 9.2mg/kg (range: 8.3- 10.5) IV qHD for average 14 days
 - Well tolerated with no elevated creatine kinase
 - All infections resolved rapidly and Cmax:MIC and AUC:MIC within optimal bactericidal range

Back to MS



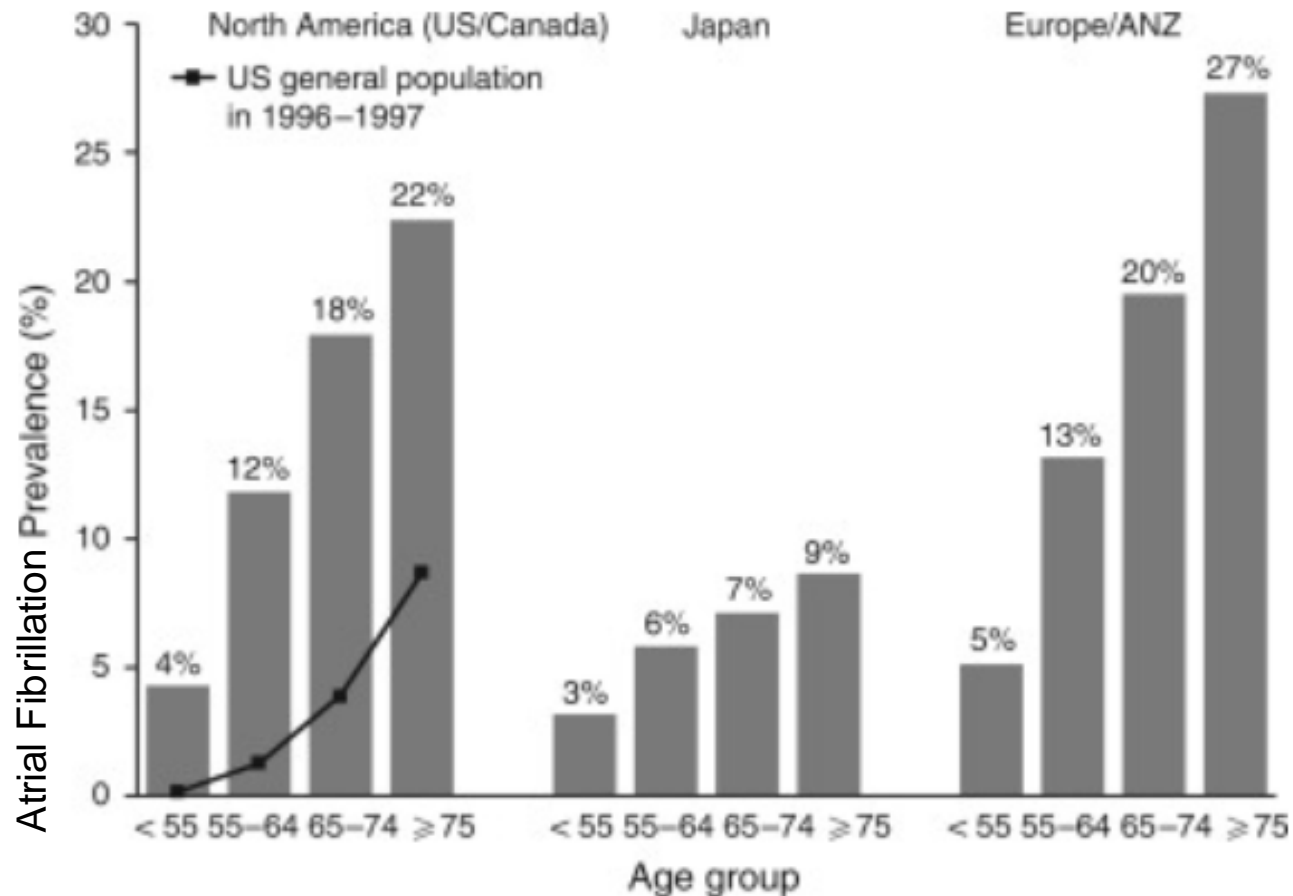
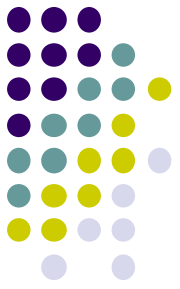
- Blood cx: 2/2 MSSA (final)
- TEE: negative for infective endocarditis (IE)
- Catheter removal booked in 2 days
- In meantime
 - Discontinue vancomycin and sodium ferric gluconate
 - Start cefazolin 2g IV qHD for 3 weeks
 - assuming fever resolved within 72hrs
 - Give cefazolin 5mg/mL +heparin 2500 units/mL catheter lock solution until catheter is removed

Medical Problem List

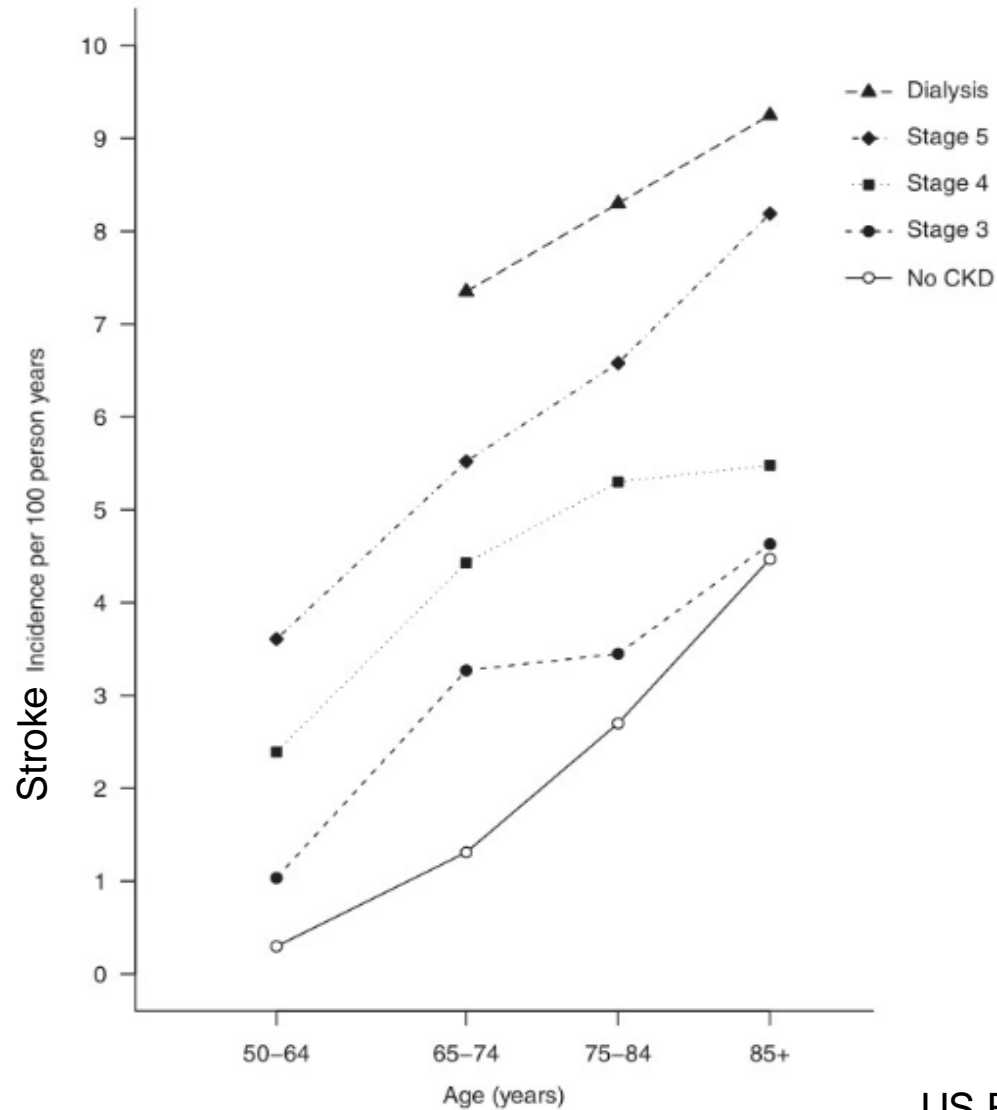


- ~~Catheter Infection~~
- New? Atrial Fibrillation
- Hypertension
- Anemia

Atrial Fibrillation (AF) in HD



Incidence of stroke in CKD



Anticoagulation - Guidelines



AHA/ACC/HRS 2019 – Class B-NR

“Might be reasonable” to prescribe warfarin or apixaban for patient on dialysis, CHA₂DS₂-VASc score ≥ 2 in men, ≥ 3 in women

KDIGO: CV and CKD controversies conference

There is insufficient data to recommend warfarin routinely for preventing stroke

Despite available dosing recommendations for apixaban and rivaroxaban, there is insufficient data on effectiveness or safety

ESC in collaboration with EACTS

Evidence for benefits... limited and controversial

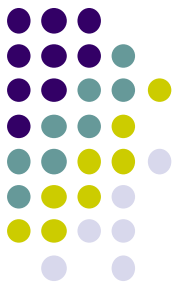
NOACs have not been approved in Europe for patients with CrCl ≤ 15 mL/min or on dialysis

Anticoagulation: Warfarin



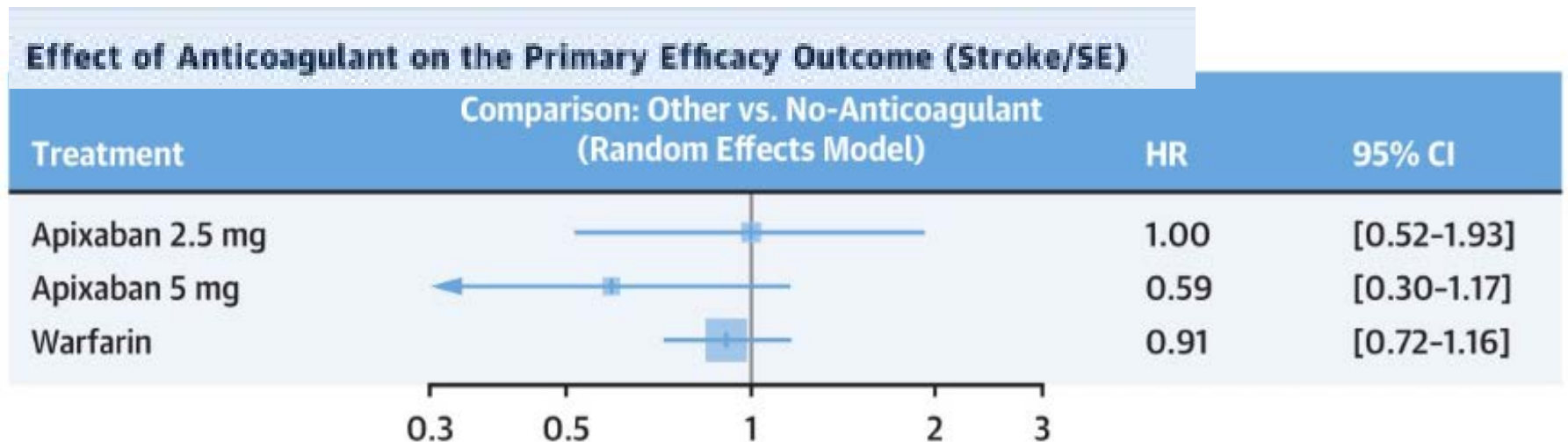
- Warfarin is used by many AF patients worldwide
- 12 meta-analyses for use in HD patients performed
 - 10 showed no reduction in ischemic strokes when warfarin was used in dialysis patients with AF
 - Most had significantly higher rates of hemorrhagic strokes and bleeding

Hart RG et al. *Ann Intern Med.* 2007; 146(12):857-67
Liu G et al. *Medicine (Baltimore).* 2015; 94(50): e2233
Dahal K et al. *Chest.* 2016; 149(4):951-9
Lee M et al. *Medicine (Baltimore).* 2016; 95(6):e2741.
Nochaiwong S et al. *Open Heart.* 2016; 3(1):e000441
Tan J et al. *BMC Nephrol* 2016; 17(1):157
Wong CX et al. *Am J Cardiol.* 2016; 117(12):1934-41
Harel Z et al. *Can J Cardiol* 2017; 33(6):737-46.
Van Der Meersch H et al. *Am Heart J* 2017; 184:37-46
Lei H et al. *Front Pharmacol.* 2018; 9:1218
Zimmerman D et al. *Nephrol Dial Transplant.* 2012; 27(10):3816-22
Kuno T et al. *J Am Coll Cardiol* 2020;75:273-85
Randhawa MS et al. *JAMA* 2020; 3(4):e202175



Kuno et al Jan 2020

- Objective: efficacy and safety of OAC for HD patients with AF
 - 16 articles; n=71,877
- Network meta-analysis performed
 - OACs not associated with lower risk of stroke and/or VTE compared with no OAC (I^2 : 70.7% p<0.0001)



Randhawa MS et al JAMA Apr 2020



- Objective: Role of warfarin in preventing ischemic strokes in ESRD patients with AF
- Systematic Review: 15 articles; n= 47,480

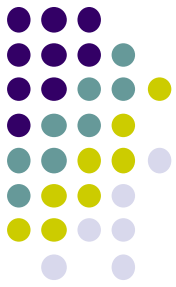
Outcome	Hazard ratio (95% CI)	I ²
Ischemic Stroke (11 studies)	0.96 (0.82-1.13)	52.6%
Hemorrhagic Stroke (7 studies)	1.46 (1.05-2.04)	37.0%
Major bleed (9 studies)	1.20 (0.99-1.47)	66.0%
Mortality (9 studies)	0.95 (0.832 – 1.09)	85.3%

Warfarin Summary



- Recent meta-analyses show **no significant benefit** from warfarin vs no OAC with respect to ischemic stroke
- **Higher major bleeding** with VKA compared to no OAC
- Inconsistencies with study design, endpoint definitions, measurements of clinical efficacy and quality preclude firm conclusions

Warfarin – AVKDIAL study



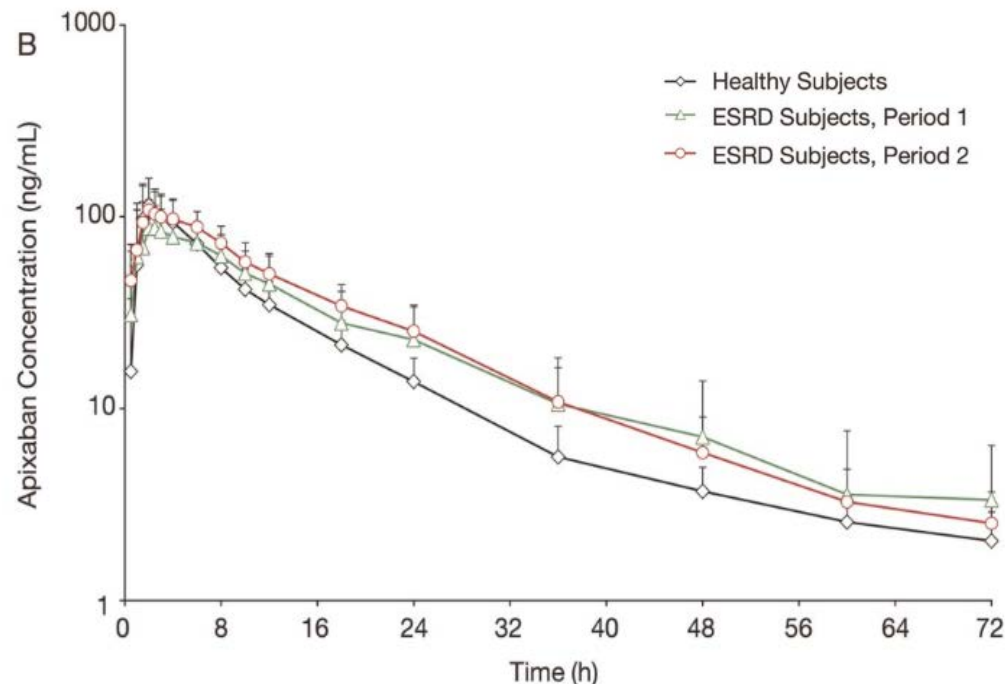
	Plan n	Study design	Intervention	Comparator	Primary outcome	Status
AVKDIAL France NCT 02886962	855	R, OL NVAF ¹ pt on HD CHA ₂ DS ₂ VASc ≥2 and HASBLED≥3 or recent bleed	No OAC	Vitamin K antagonist adjusted to INR 2-3	Cumulative incidence of severe bleed and thrombosis	Recruiting Est complete Jan 2023

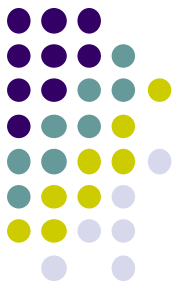
1. NVAF Nonvalvular atrial fibrillation

Anticoagulation: Apixaban



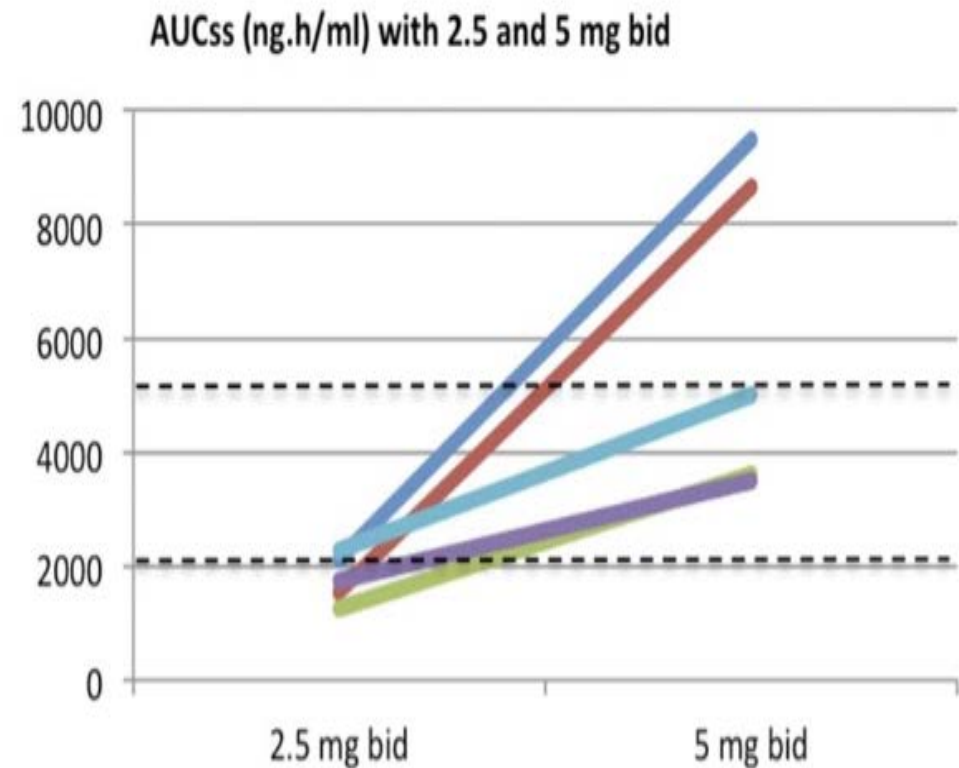
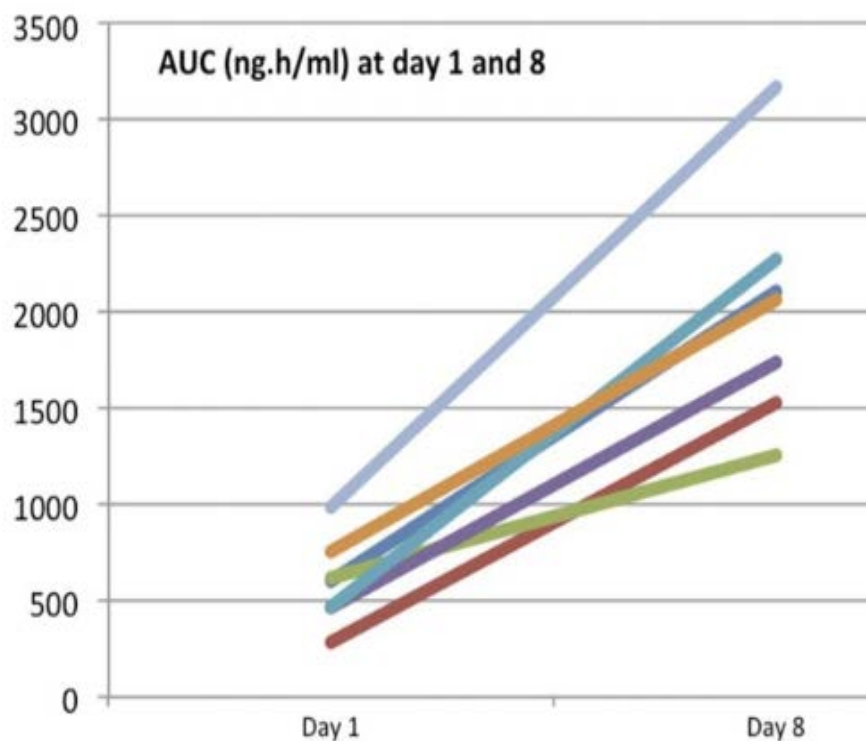
- US FDA approved use in HD patients since April 2013
 - Pharmacokinetic data study by Wang et al
 - n= 16 (8 HD and 8 healthy patients), single dose of apixaban 5mg
 - After 4 hrs of HD, 6.7% of dose was removed by dialysis





Anticoagulation: Apixaban

- Phase 1 (n=7): Apixaban 2.5mg BID 8 days; 5 day washout
- Phase 2 (n=5): Apixaban 5mg BID 8 days



Apixaban in AF HD trials



	Design	N	Apixaban	Warfarin	Outcomes
Stanton et al. Pharmacotherapy. 2017	R, matched 1:1 Jan 2014 – Dec 2015	n= 146 (40 RRT) (73% for NVAF)	73 (19 HD)	73 (19 HD)	HD pt, major bleed and composite bleed NSS (p=0.663 and p=0.549, respectively) 4 stroke events in each group for patients being treated for NVAF
Reed et al Res Pract Thromb Haemost. 2018	R cohort Jan 2014 – Oct 2016	124 RRT (39% for NVAF)	74 (80% received Apix 5mg BID)	50	Overall bleed OR 0.15 (0.05-0.46) p=0.001 Major bleed (5.4% vs 22% p=0.1) No recurrent ischemic stroke in either
Siontis et al. Circulation 2018	R cohort USRDS Oct 2010 - Dec 2015	25,523 RRT pt with NVAF	2,351 (44% received Apix 5mg BID)	23,172	NSS stroke (p=0.29) ↓ major bleed (HR0.72[0.59-0.87]; p<0.001) NSS ↓ mortality (HR0.85[0.71-1.010]; p=0.06) Sensitivity analysis showed apix 5mg BID had SS ↓ stroke, embolism and death compared with apix 2.5mg BID and warfarin

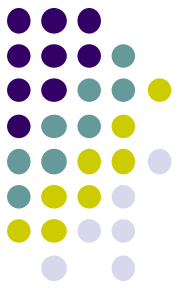
RENAL-AF



Design	RCT, OL with blinded event adjudication
Inclusion	HD patient with nonvalvular AF, CHA ₂ DS ₂ VASc ≥ 2
Exclusion	ASA > 81 mg, need for DAPT, OAC for non-AF indication
Intervention	Apixaban 5mg BID (dose reduction to 2.5mg BID for selected patients)
Comparator	Warfarin adjusted to INR 2-3
Study stopped early due to funding issues. Recruited only 155 patients (planned 760). Slower than anticipated enrollment due to patient and dialysis center factors	

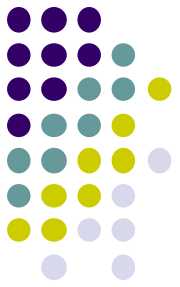
- Full paper unpublished.
 - Information presented at AHA Nov 2019 by Pokorney SD

RENAL-AF – Baseline



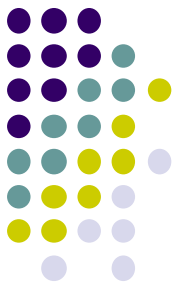
	Apixaban (n=82)	Warfarin (n=72)
Age, median (IQR)	69 (61, 76)	68 (61, 73)
≥ 75 yo	24 (29.3%)	15 (20.8%)
Female	34 (41.5%)	22 (30.6%)
CHA ₂ DS ₂ VASc, median (IQR)	4.0 (3.0, 5.0)	4.0 (3.0, 5.0)
Stroke history	17 (20.7%)	12 (16.7%)
Warfarin or NOAC naïve	10 (12.2%)	4 (5.6%)
Prior clinically relevant/spontaneous bleeding	18 (22.0%)	14 (19.4%)
Bleeding within 1yr requiring hospital	8 (9.8%)	2 (2.8%)
Concurrent ASA	29 (36.7%)	32 (45.7%)

RENAL-AF – Dosing



Pt randomized to apixaban	Apixaban (n=77)
Initial apixaban dose	
2.5 mg BID	22 (28.6%)
5 mg BID	55 (71.4%)
apixaban dose reduced from 5 mg to 2.5 mg	15 (27.3%)
Pt randomized to warfarin	Warfarin n=68
TTR	44.3% (23.2 – 59%)

- Pt were **three** times likely to be subtherapeutic than suprathereapeutic
- Only 68% of patient in each arm completed study



RENAL-AF - Outcomes

- 1°: ISTH major or clinically relevant non-major bleed @ 12mo
 - ITT: HR 1.20 (95% CI 0.63, 2.30)

	Apixaban (n=82)	Warfarin (n=72)
ISTH major bleed/clinically relevant non-major bleed	21 (25.6%)	16 (22.2%)
intracranial	1 (1.2%)	1 (1.4%)
Gastrointestinal	2 (2.4%)	6 (8.3%)
Hemodialysis access site	11 (13.4%)	6 (8.3%)
ISTH major bleed	7 (8.5%)	7 (9.7%)
intracranial	1 (1.2%)	1 (1.4%)
Gastrointestinal	2 (2.4%)	5 (6.9%)
Hemodialysis access site	1 (1.2%)	0 (0.0%)
ISTH clinically relevant non-major bleed	14 (17.1%)	9 (12.5%)
Gastrointestinal	0 (0.0%)	1 (2.8%)
Hemodialysis access site	10 (12.2%)	6 (8.3%)

RENAL-AF - Outcomes



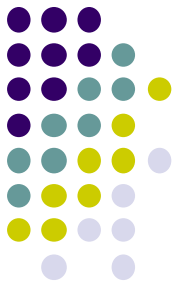
	Apixaban (n=82)	Warfarin (n=72)
Stroke	2 (2.4%)	2 (2.8%)
Ischemic	1 (1.2%)	2 (2.8%)
Hemorrhagic	1 (1.2%)	0 (0.0%)
Systemic embolism	0 (0.0%)	0 (0.0%)
Death	21 (25.6%)	13 (18.1%)
Cardiovascular	9 (11.0%)	4 (5.6%)
Non-cardiovascular	5 (6.1%)	8 (11.1%)
Undetermined	7 (8.5%)	1 (1.4%)
Bleeding related death	1	0 (0%)

RENAL-AF - Conclusions



- Author's conclusion:
 - Apixaban 5mg BID similar bleeding and stroke rates as warfarin
 - Unclear if lower dose (2.5mg BID) and cessation of ASA would have resulted in lower bleeding compared to warfarin
- Limitations
 - Warfarin TTR 44% - large proportion in subtherapeutic range
 - Lack of power - premature termination of study
 - Unbalanced baseline

Apixaban vs no anticoagulation



Design	Retrospective cohort using US Renal database 2012-2015
Inclusion	HD patient with incident nonvalvular AF treated with Apixaban matched (1:3) with patients not treated with any anticoagulant
Exclusion	Use of OAC 6mo prior to AF diagnosis
Intervention	n= 521; Apixaban 5mg BID (40%), 2.5mg BID (49%), switched (11%)
Comparator	n= 1,561; No OAC

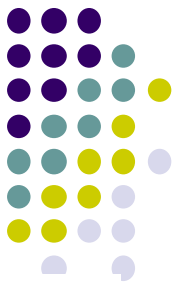


Mavrakanas et al 2020

Table 2. Clinical outcomes in the “as-treated” population (main analysis)

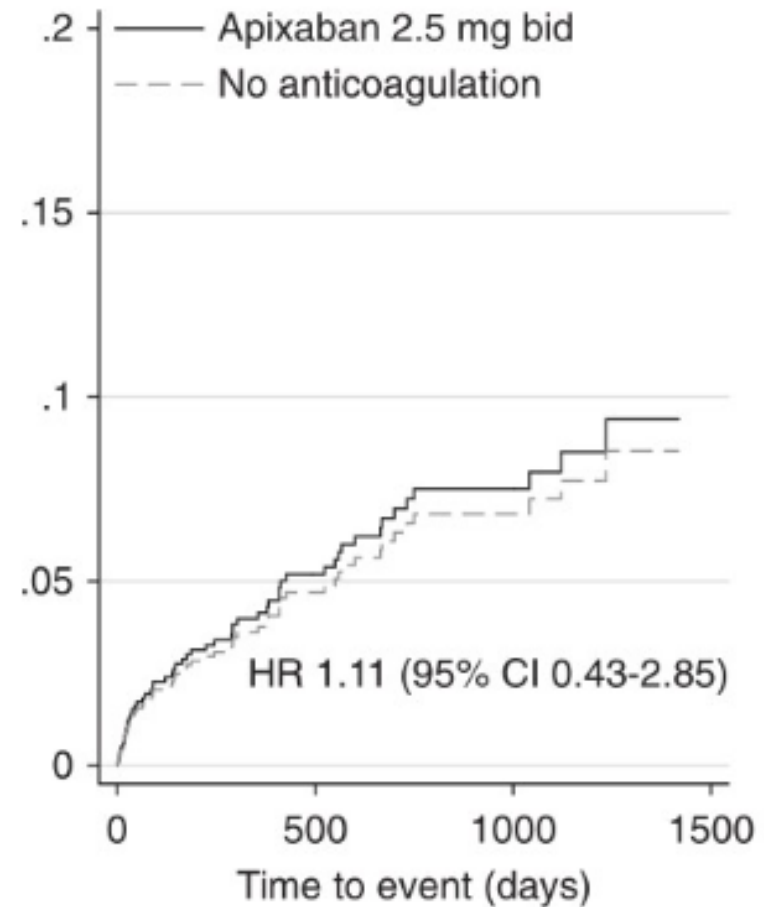
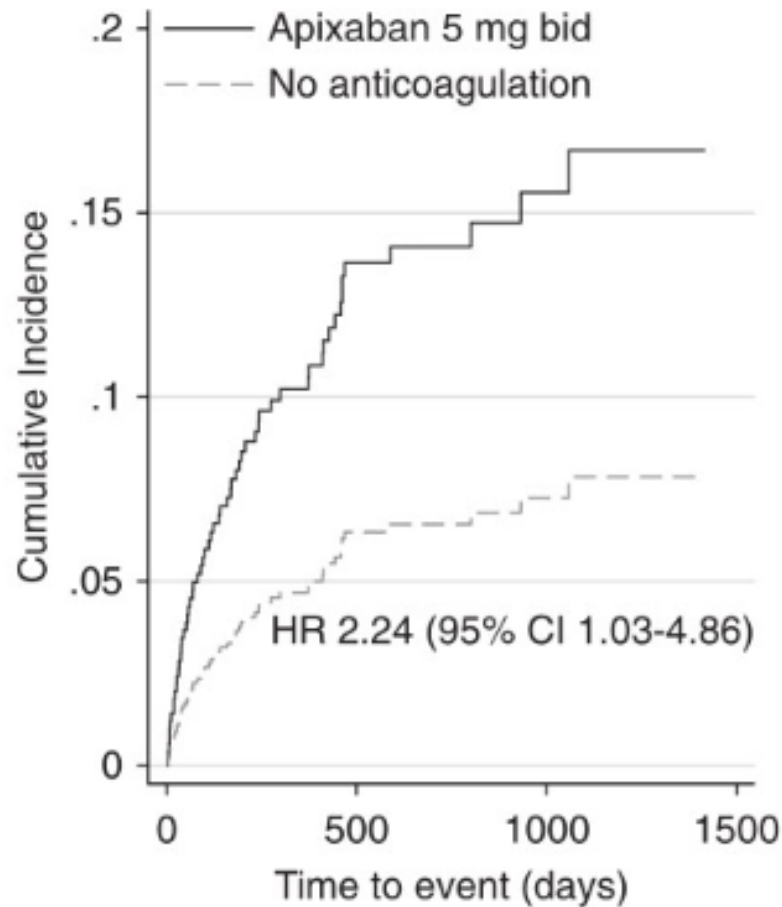
Outcome	Incidence in Apixaban Users	Incidence in Nonusers	Crude Hazard Ratio (95% Confidence Interval)	P Value	Adjusted ^a Hazard Ratio (95% Confidence Interval)	P Value
Any stroke, TIA, or embolism	7.5 (13)	7.0 (114)	1.24 (0.69 to 2.23)	0.47	1.29 (0.72 to 2.33)	0.39
Any stroke	5.8 (<11)	5.8 (96)	1.13 (0.58 to 2.19)	0.72	1.17 (0.60 to 2.28)	0.64
Major bleeding	4.9 (<11)	1.6 (45)	2.74 (1.37 to 5.47)	0.004	2.76 (1.38 to 5.52)	0.004
Clinically important bleeding	59.2 (77)	56.9 (695)	1.15 (0.90 to 1.47)	0.26	1.15 (0.90 to 1.46)	0.26
Ischemic stroke or MI	27.6 (43)	25.1 (373)	1.24 (0.90 to 1.71)	0.18	1.25 (0.91 to 1.72)	0.17
Ischemic stroke	3.5 (<11)	5.0 (81)	0.81 (0.35 to 1.89)	0.63	0.85 (0.36 to 1.98)	0.71
Hemorrhagic stroke	2.3 (<11)	1.3 (22)	1.89 (0.65 to 5.47)	0.24	1.89 (0.65 to 5.49)	0.24

- 2^o outcome:
 - All cause mortality HR 0.58; 95% CI, 0.43 to 0.78
 - All cause mortality or stroke or systemic thromboembolism HR 0.56; 95% CI, 0.41 to 0.76

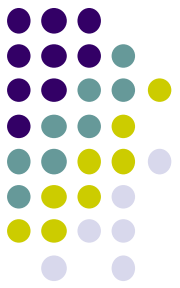


Mavrakanas et al 2020

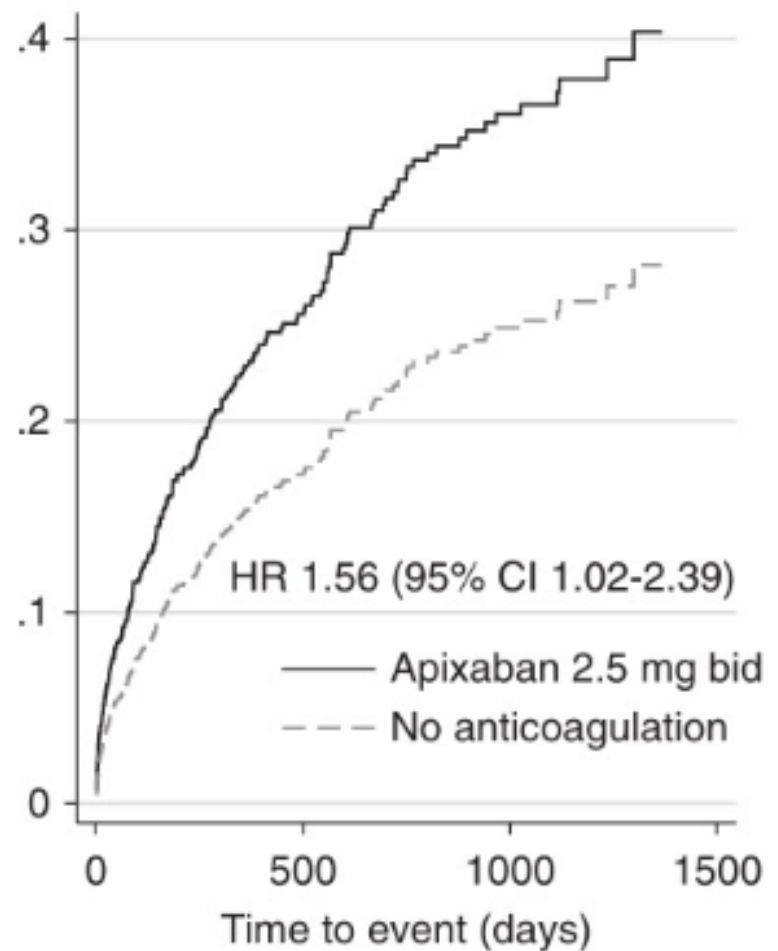
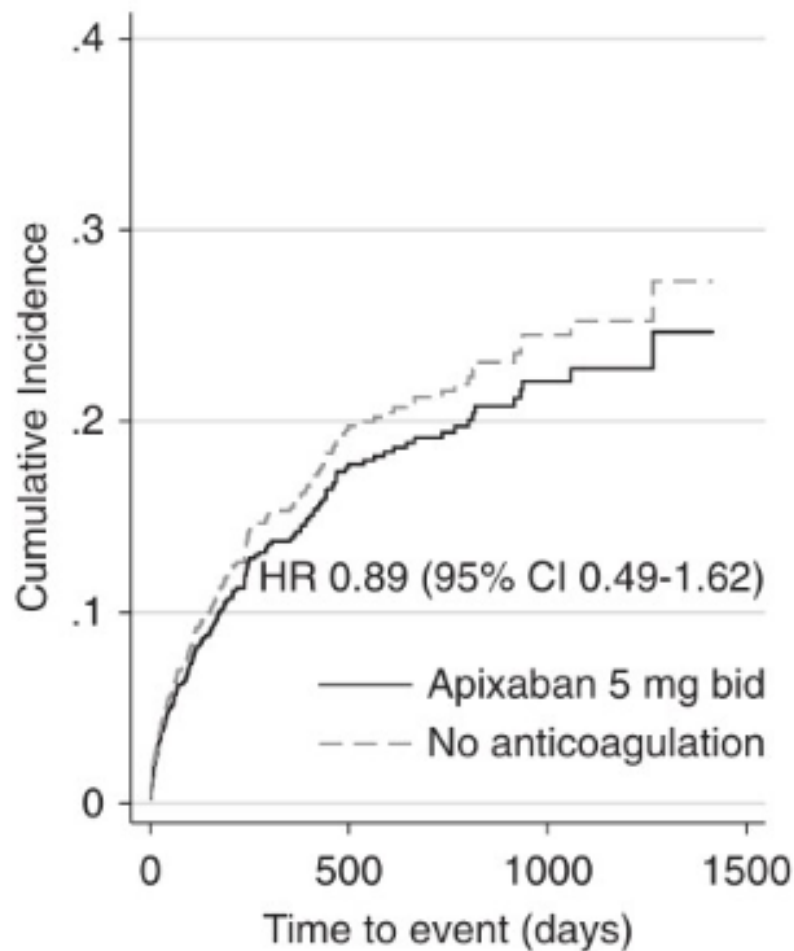
Any stroke or TIA or systemic embolism

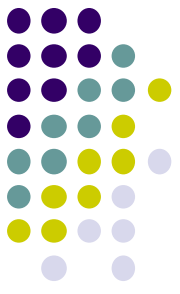


Mavrakanas et al 2020



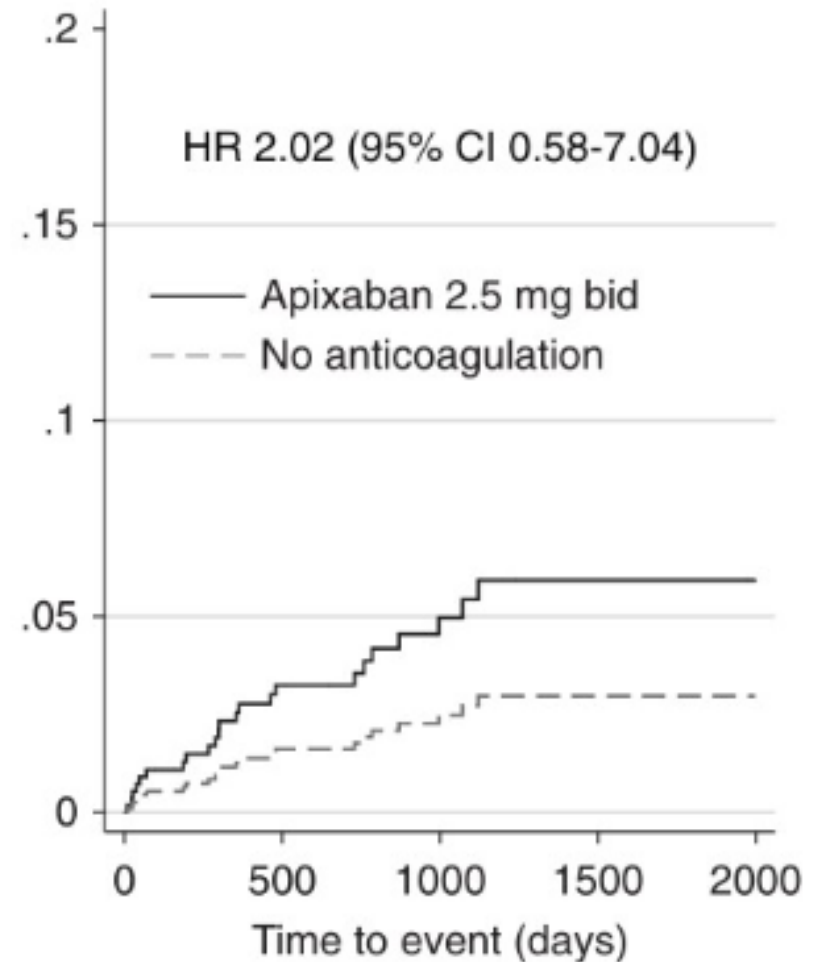
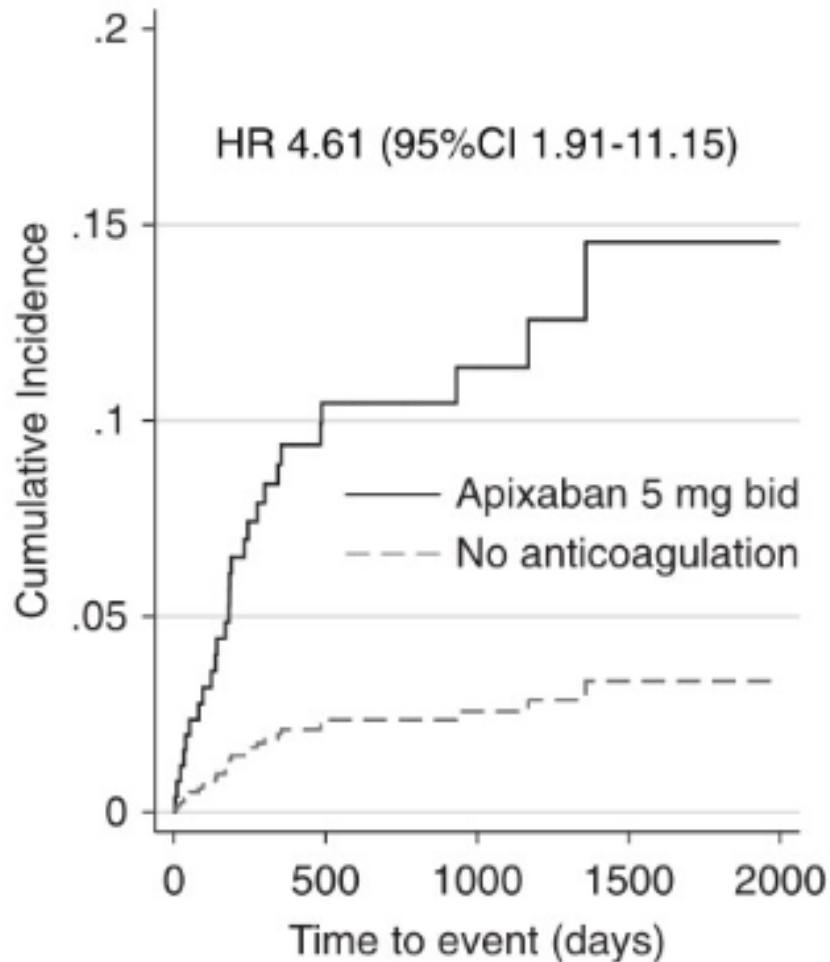
Ischemic stroke or MI

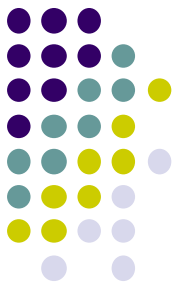




Mavrakanas et al 2020

Fatal or intracranial bleeding





Mavrakanas et al 2020

- Sensitivity analysis using pneumonia and hip fracture show a selection bias for healthier patients in apixaban group
- Apixaban 5mg BID had NSS reduction in ischemic strokes
 - Significantly higher risk of fatal or intracranial bleed and hemorrhagic stroke compared with no treatment
- Confounders such as BP control, BMI, concomitant prescriptions or anticoagulant use during dialysis were not collected

Upcoming Apixaban trials

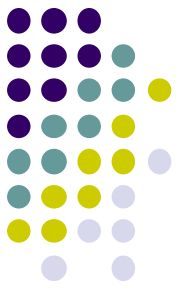


	Plan n	Study design	Intervention	Comparator		Primary outcome	Status
SAFE-D Canada NCT 03987711	150	R, OL NVAF pt on HD CHADS-65	Apixaban 5mg BID (can reduce to 2.5mg BID)	Warfarin daily INR 2-3	No OAC	Recruitment of target within 2yrs and 80% of randomized pt remain at end of 26 week study	Recruiting Est complete Dec 2021
AXADIA Germany NCT 02933697	222	R, OL NVAF pt on HD CHA ₂ DS ₂ VASc ≥2	Apixaban 2.5mg BID	Phenprocoumon adjusted to INR 2-3		Incidence of major/clinically relevant nonmajor bleed	Recruiting Est complete Jul 2022

Back to MS



- Incidental Afib
- Indication for OAC?
 - $CHA_2DS_2VASc = 6$ (HTN, Age >75, T2DM, Stroke)
 - AHA/ACC/HRS recommends treatment for men if score ≥ 2



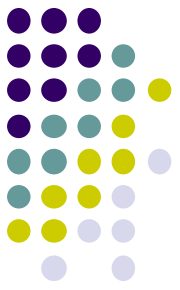
Bonde AN et al. JACC 2014

- Nationwide Danish registry
 - All patients discharged with NVAF from 1997-2011
 - 1^o outcome: hospitalization from stroke/TE (peripheral arterial embolism, ischemic stroke, transient ischemic attack)

TABLE 2 Rates (95% CI; Number of Events) of Stroke and TE per 100 Person-Years In Patients With AF According to Renal Status, Warfarin Treatment, and CHA₂DS₂-VASc Score

CHA ₂ DS ₂ -VASc Score	No CKD		Non-End-STAGE CKD		RRT	
	Not Receiving Warfarin (n = 96,479*)	Receiving Warfarin (n = 52,119*)	Not Receiving Warfarin (n = 3,389*)	Receiving Warfarin (n = 1,130*)	Not Receiving Warfarin (n = 882*)	Receiving Warfarin (n = 260*)
0	0.8 (0.7-0.8; 446)	0.7 (0.6-0.9; 149)	2.1 (0.9-3.4; 11)	1.3 (0.0-3.7; 3)	4.2 (1.5-6.9; 9)	0
1	1.4 (1.4-1.5; 966)	1.0 (0.9-1.1; 358)	1.5 (0.9-2.2; 19)	1.8 (0.7-2.8; 11)	2.8 (1.6-4.1; 21)	3.3 (0.8-5.7; 7)
≥2	5.3 (5.2-5.4; 13,622)	2.9 (2.8-3.0; 4336)	7.2 (6.7-7.7; 763)	5.8 (5.1-6.4; 280)	7.3 (6.2-8.5; 156)	4.8 (3.2-6.4; 34)

- Warfarin had SS net clinical benefit
- Warfarin had trend toward lower risk of all-cause mortality and CV death



Anticoagulation

- Studies identifying stroke risk factors in HD pt with Afib

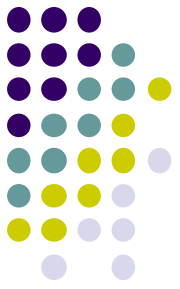
	C	H	A ₂	D	S ₂	V	A	Sc
Iseki (1996)		X						
Seliger (2003)		X	X					
Delmez (2006)				X				
Chan (2009)	X	X		X	X		X	
Sozio (2009) Afib			X	X				
Tripepi (2010)								
Sanchez-Perales (2010) Afib			X	X				
Shoji (2011)			X	X				X
Olesen (2012)			X		X			
Power (2012) Afib				X	X			
Wang (2014)		X	X	X				



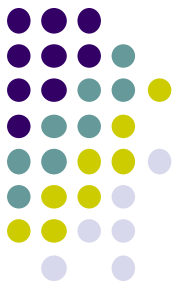
Back to MS

- Incidental Afib
- Indication for OAC?
 - $CHA_2DS_2VASc = 6$
- With current evidence, patient is at significant risk for stroke recurrence and OAC should be discussed with patient
 - Warfarin
 - HD patients excluded in many of early studies
 - Recent meta-analyses have shown lack of efficacy in reducing ischemic strokes and increase in significant bleeds
 - Questionable quality and heterogeneous evidence meta-analyzed
 - Apixaban
 - Uncertain efficacy: current evidence has not shown apixaban to be beneficial over no OAC or warfarin

Poll



- What would you do?
 - Recommend warfarin
 - Recommend apixaban 5mg po BID
 - Recommend apixaban 2.5mg po BID
 - Do not recommend anticoagulation but counsel patient of other strategies to reduce stroke risk



My personal approach

- In HD patients with newly diagnosed Afib

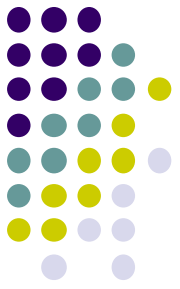
CHA ₂ DS ₂ VASc score		Recommendation
Men	Women	
<1	<2	No anticoagulation
2-3	3-4	Review risk factors <ul style="list-style-type: none">• Less weight if risk factors were CHF, Vascular disease and age 65-74• If patient has hypertension – would consider only if it is still uncontrolled
≥ 4	≥ 5	Offer anticoagulation with counseling of risks



Back to MS

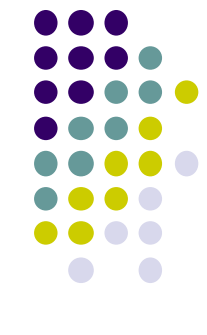
- Incidental Afib
- Indication for OAC?
 - $CHA_2DS_2VASc = 6$
- Would recommend, discontinue ASA and start warfarin
 - Years of experience and patient on HD, can closely monitor INR
 - Warfarin can be quickly reversed for any emergency procedures
 - Apixaban for this indication is not covered; Pharmacare excludes CrCl <25ml/min

Medical Problem List



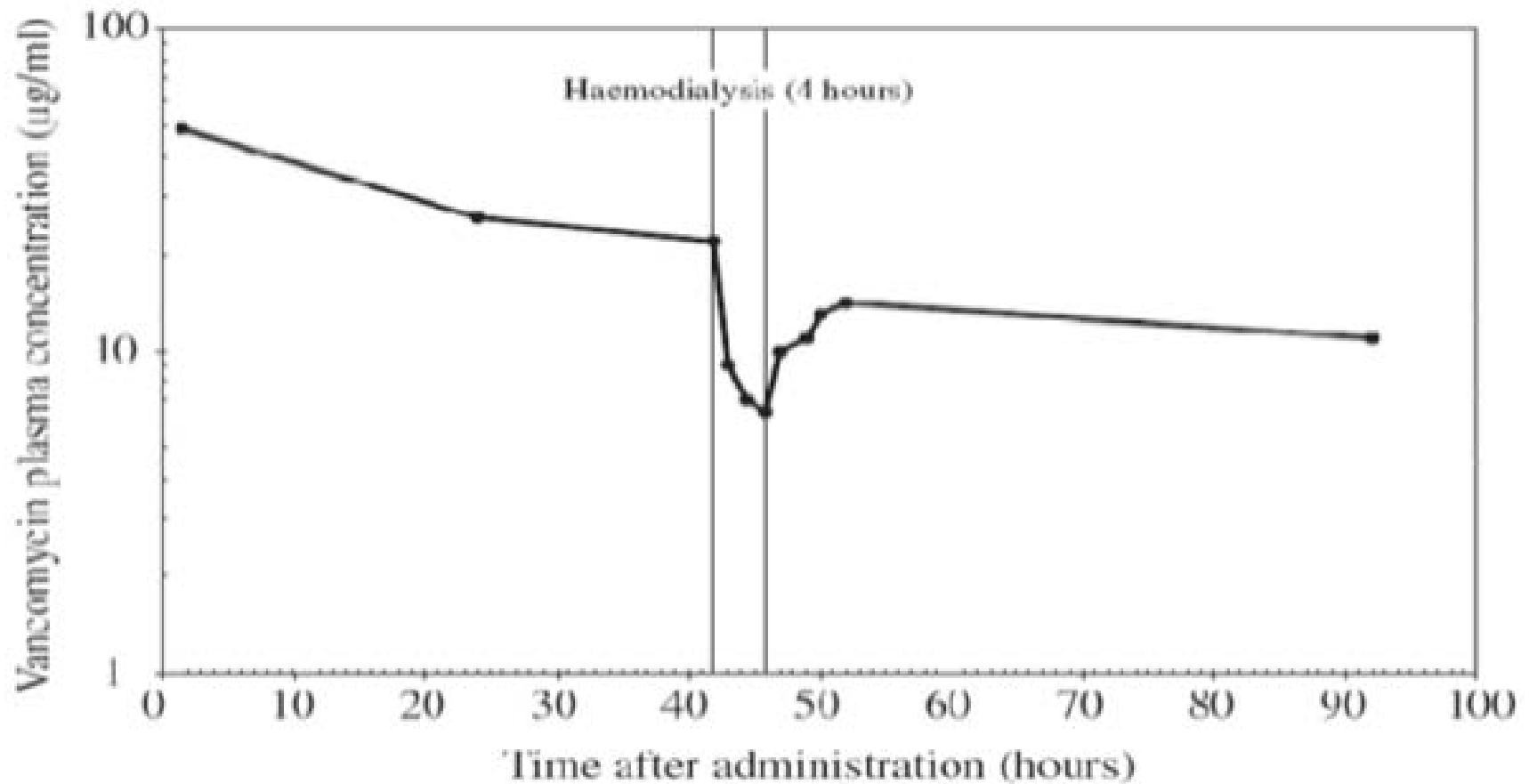
- ~~Catheter Infection~~
- ~~New? Atrial Fibrillation~~
- Hypertension
- Anemia

Next time....



Questions?

Vancomycin in hemodialysis



Catheter related infection



- Catheter salvage has highest risk of treatment failure (compared to catheter replacement)
 - Treatment failure @ 6mo 33% vs 8% $p < 0.001$
 - Catheter removal when (IDSA 2009 LOE A-II)
 - Severe sepsis, endocarditis, metastatic infection
 - Persistent bacteremia after >72hrs of susceptible abx
 - Infections due to *s. aureus*, *p. aeruginosa*, fungi, mycobacteria