AFD atriyal fibrilasyon derneği
7. Atriyal Fibrilasyon Zirvesi 2018
9 - 10 Şubat 2018
Kempinski Hotel The Dome
Belek, Antalya

AF ABLASYONU SIRASINDA ANTİKOAGÜLASYON YÖNETİMİ

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İşlem Öncesi Embolizasyon Nedenleri

- ✓ Kateter ablasyonu sırasında Stroke, TİA ve diğer embolizasyon oranı % 0.4- 2.0
- ✓ Çoğu inme vakaları genellikle işlemden 24-48 saat içinde ortaya çıkmaktadır.Birinci haftada ortaya çıkan emboli vakaları bildirilmiştir.

AF Ablasyonu Sırasında Tromboembolizm Nedenleri

- ✓ İşlem öncesi antikoagülasyonun kesilmesi
- ✓ Kateter ile trombusun yerinden oynatılması
- ✓ Kateter travmasına bağlı sol atriyal hasar ve endotelde gelişen trombusEndoteliyal bozulma,fibrozis ,skar
- ✓ Kateter içinde trombus varlığı
- ✓ Bazı hastalarda işlem sırasında sinüs ritmine döndürmek için kardioversiyon sonrası
- ✓ Atriyal "stunning"
- ✓ Çok sayıda intraatriyal kateter ve sheatler
- ✓ Koagulasyon faktörlerinin aktivasyonu

Pre-Postablasyon Tromboemboli Riski

- ✓CHADS2 skoru ≥ 2
- ✓İnme öyküsü
- ✓Persistan AF
- ✓Sol Atriyal genişliği
- ✓Sol Atriyal Apendiks dilatasyonu

✓% 0.5-2.8

Tromboemboli

- ✓ Serebroembolik olay: 1-5%
- ✓ Ablasyon esnasında TCD ile çok sayıda "mikroembolik sinyal" tespit edilmektedir.
  - ✓ Ablasyon esnasında çok sayıda mikroembolizasyon olmaktadır. Ancak bunların çoğu önemli klinik sorun oluşturmayan mikrobubble'lardır.

Sessiz İnme

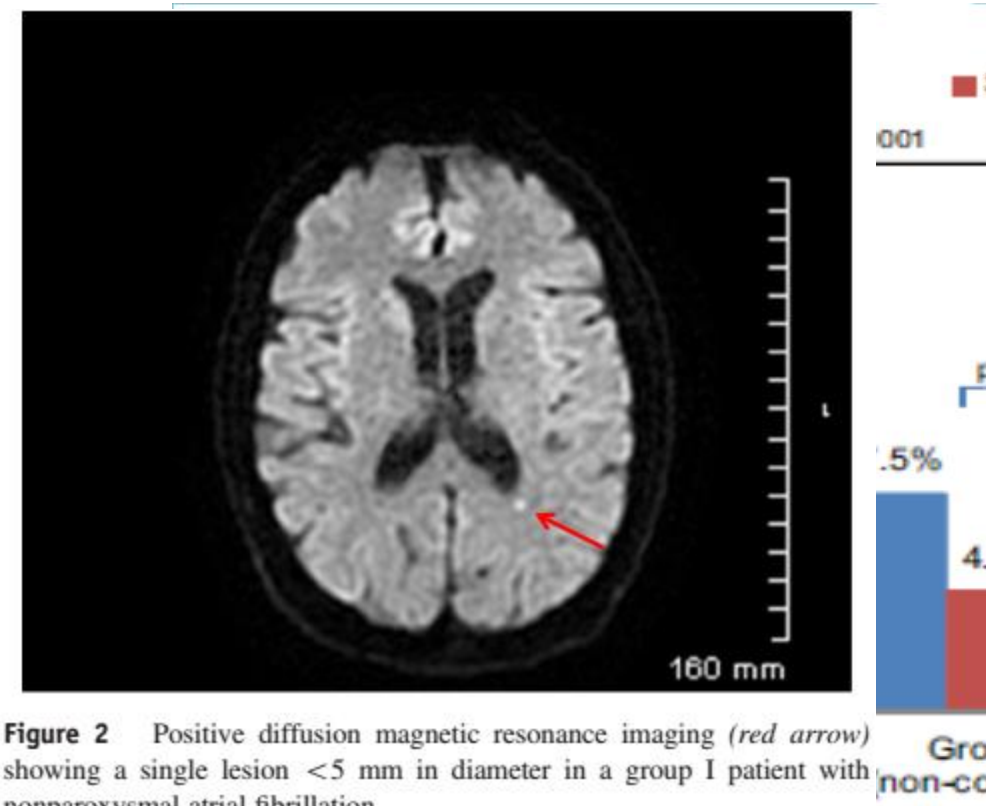


Figure 2 Positive diffusion magnetic resonance imaging *(red arrow)* showing a single lesion <5 mm in diameter in a group I patient with nonparoxysmal atrial fibrillation.

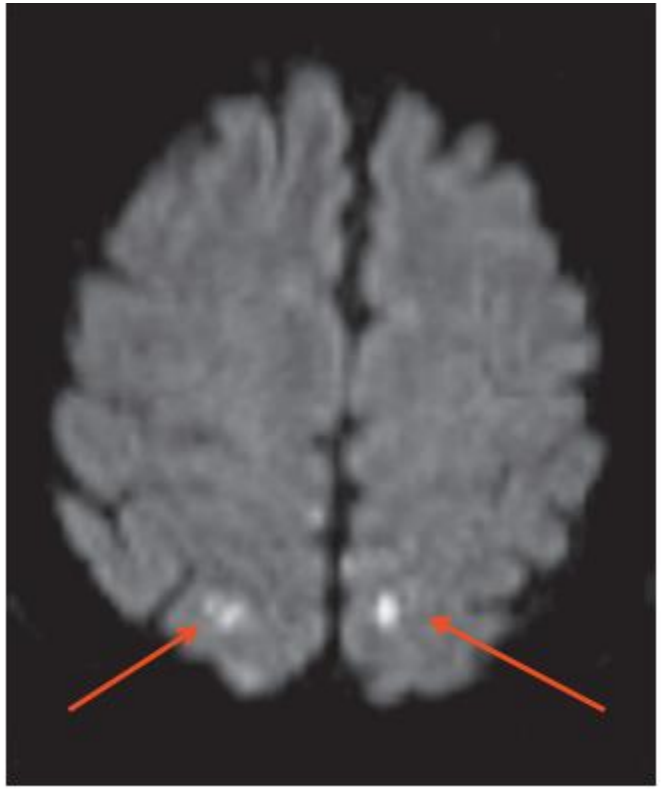


Figure 4 Bilateral parietal embolic lacunar infarct *(red arrows)* in a group III patient. Both lesions appear to be >5 mm in diameter.

Does periprocedural anticoagulation management of atrial fibrillation affect the prevalence of silent thromboembolic lesion detected by diffusion cerebral magnetic resonance imaging in patients undergoing radiofrequency atrial fibrillation ablation with open irrigated catheters? Results from a prospective multicenter study.Biase LD, Gaita F et.al. Heart Rhythm 2014;11:791-798.

	Patients with SCIL (n=40)	Patients without SCIL (n=246)	P-value
Age (years)	68 (61–72)	67 (60–72)	0.509
Male gender	28 (70.0)	180 (73.2)	0.676
Body weight (kg)	63.5±11.3	65.4±11.9	0.363
Type of AF			0.014
Paroxysmal	19 (47.5)	128 (52.0)	
Persistent	8 (20.0)	82 (33.3)	
Long-standing persistent	13 (32.5)	36 (14.6)	
Structural heart disease	3 (7.5)	33 (13.4)	0.296
Hypertension	22 (55.0)	150 (61.0)	0.474
Diabetes mellitus	6 (15.0)	40 (16.3)	0.841
Heart failure	4 (10.0)	24 (9.8)	0.572
Stroke/TIA	4 (10.0)	20 (8.1)	0.440
$CHADS_2$ score	1 (0–2)	1 (0–2)	0.914
CHA_2DS_2-VASc score	2 (1–3)	2 (1–3)	0.639
Type of OAC			0.142
Warfarin	4 (10.0)	42 (17.1)	
Dabigatran	11 (27.5)	36 (14.6)	
Rivaroxaban	8 (20.0)	81 (32.9)	
Apixaban	14 (35.0)	73 (29.7)	
Edoxaban	3 (7.5)	14 (5.7)	
>3 weeks OAC before procedure	35 (87.5)	218 (88.6)	0.504
Antiplatelet drugs	4 (10.0)	27 (11.0)	0.557
D-dimer (μg/ml)	0.3 (0.2–0.5)	0.3 (0.2–0.4)	0.500
BNP (pg/ml)	101.0 (44.8–179.3)	69.8 (33.0–141.5)	0.145
LAD (mm)	43 (37.5–48)	41 (37–45)	0.268
LVEF (%)	65 (55–65)	60 (55–65)	0.954
LAA flow velocity (cm/s)	47.5 (27–77)	52 (28–78)	0.737
Spontaneous echo contrast	13 (32.5)	62 (25.2)	0.331
Total procedure time (min)	153 (123.5–168)	138 (121–159)	0.082
Type of LA procedure			0.033
PVI alone	31 (77.5)	220 (89.4)	
PVI and substrate modification	9 (22.5)	26 (10.6)	
Type of LA ablation energy source			0.460
RF	34 (85.0)	219 (89.0)	
Cryothermal	6 (15.0)	27 (11.0)	
Total heparin dosage (units)	13,995 (12,100–15,587.5)	12,905 (11,235–15,517.5)	0.177
Mean ACT during procedure (s)	317 (304–336)	315 (303–333)	0.604
Maximum ACT during procedure (s)	336 (322–371)	338 (323–361)	0.931
Electrical cardioversion during procedure	25 (62.5)	126 (51.2)	0.185
Exchanging catheters over the transseptal sheaths	10 (25.0)	44 (17.9)	0.286

AF Ablasyonunda Antikoagülasyon

Ablasyon öncesi

Ablasyon sırasında

Ablasyon sonrasında

2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: Executive summary

Anticoagulation strategies: pre-, during, and postcatheter ablation of AF

	Recommendation	Class	LOE	References
Preablation	For patients undergoing AF catheter ablation who have been therapeutically anticoagulated with warfarin or dabigatran, performance of the ablation procedure without interruption of warfarin or dabigatran is recommended.	I	A	366–373
	For patients undergoing AF catheter ablation who have been therapeutically anticoagulated with rivaroxaban, performance of the ablation procedure without interruption of rivaroxaban is recommended.	I	B-R	374
	For patients undergoing AF catheter ablation who have been therapeutically anticoagulated with a NOAC other than dabigatran or rivaroxaban, performance of the ablation procedure without withholding a NOAC dose is reasonable.	IIa	B-NR	375
	Anticoagulation guidelines that pertain to cardioversion of AF should be adhered to in patients who present for an AF catheter ablation procedure.	I	B-NR	5,6
	For patients anticoagulated with a NOAC prior to AF catheter ablation, it is reasonable to hold one to two doses of the NOAC prior to AF ablation with reinitiation postablation.	IIa	B-NR	372,376–380
	Performance of a TEE in patients who are in AF on presentation for AF catheter ablation and who have been receiving anticoagulation therapeutically for 3 weeks or longer is reasonable.	IIa	C-EO	5,6
	Performance of a TEE in patients who present for ablation in sinus rhythm and who have not been anticoagulated prior to catheter ablation is reasonable.	IIa	C-EO	5,6
	Use of intracardiac echocardiography to screen for atrial thrombi in patients who cannot undergo TEE may be considered.	IIb	C-EO	381–386
During ablation	Heparin should be administered prior to or immediately following transseptal puncture during AF catheter ablation procedures and adjusted to achieve and maintain an ACT of at least 300 seconds.	I	B-NR	369,380–382,387–393
	Administration of protamine following AF catheter ablation to reverse heparin is reasonable.	IIa	B-NR	394
Postablation	In patients who are not therapeutically anticoagulated prior to catheter ablation of AF and in whom warfarin will be used for anticoagulation postablation, low molecular weight heparin or intravenous heparin should be used as a bridge for initiation of systemic anticoagulation with warfarin following AF ablation.*	I	C-EO	
	Systemic anticoagulation with warfarin* or a NOAC is recommended for at least 2 months postcatheter ablation of AF.	I	C-EO	1,2
	Adherence to AF anticoagulation guidelines is recommended for patients who have undergone an AF ablation procedure, regardless of the apparent success or failure of the procedure.	I	C-EO	5,6
	Decisions regarding continuation of systemic anticoagulation more than 2 months post ablation should be based on the patient's stroke risk profile and not on the perceived success or failure of the ablation procedure.	I	C-EO	5,6
	In patients who have not been anticoagulated prior to catheter ablation of AF or in whom anticoagulation with a NOAC or warfarin has been interrupted prior to ablation, administration of a NOAC 3 to 5 hours after achievement of hemostasis is reasonable postablation.	IIa	C-EO	372,376–380
	Patients in whom discontinuation of anticoagulation is being considered based on patient values and preferences should consider undergoing continuous or frequent ECG monitoring to screen for AF recurrence.	IIb	C-EO	

AF = atrial fibrillation; LOE = Level of Evidence; NOAC = novel oral anticoagulant; TEE = transesophageal electrocardiogram; ACT = activated clotting time.

* Time in therapeutic range (TTR) should be > 65% – 70% on warfarin

Journal of Arrhythmia 33 (2017) 369–409

AF Ablasyonundan Önce Antikogülasyon

Preablasyon TEE

- ✓ Persistan AF olan veya embolik riski yüksek olan hastalarda ablasyon öncesinde TEE veya başka metodlarla intrakardiyak trombüs araştırması önerilmektedir.
- ✓ Eğer ablasyondan öncesi 4 hafta INR terapötik düzeydeyse işlem öncesinde sinüs ritminde olan hastalarda TEE gerekmeyebilir.
  - ✓ 48 saattten uzun süreli veya süresi bilinmeyen AF'de işlemden önce en az 3 hafta terapötik seviyede antikoagülasyon yapılmamışsa (sınıf I)
  - ✓ İşlem sırasında sinüs ritmindeki hastalarda veya AF süresi 48 saatten daha kısa olanlarda TEE düşünülebilir (sınıf IIa)

İşlem öncesi antikoagülasyon-I

- ✓ İşlem öncesi antikoagülasyon:
  - ✓ AF süresi >48 saat veya bilinmiyorsa en az 3 hafta terapötik seviyede antikoagülasyon veya (sınıf I)
  - ✓ İşlem öncesi en az 3 hafta antikoagülasyon söz konusu değilse TEE ile trombüsün dışlanması (sınıf I)
  - ✓ Sol atriyumda trombüs varlığı kateter ablasyonu için kontrendikasyondur (sınıf III)

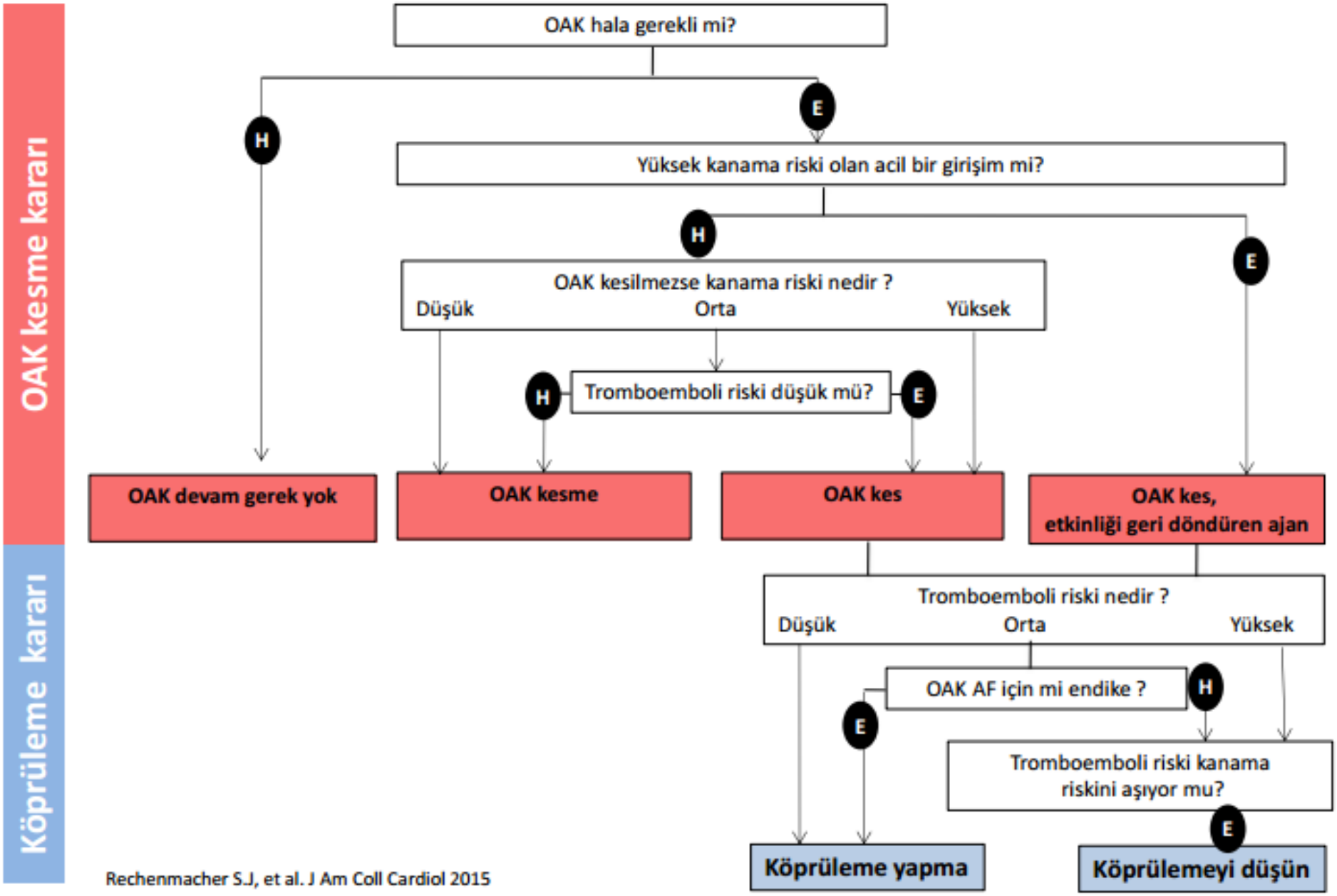
İşlem öncesi antikoagülasyon-II

- ✓ Warfarinin Kesilmesi
  - ✓ Warfarinin işlem öncesi kesilip heparine geçilmesi, işlem sırası ve sonrasında heparin kullanılması (giriş yeri kanamasında artış !)
- ✓ İşlemin Warfarinin altında yapılması
  - ✓ İşlemin terapötik seviyede kullanılan warfarin altında yapılması (ACC/AHA/HRS 2014)
- ✓ YOAK kesilmesi
  - ✓ kullananlarda işlem öncesi dabigatran ve apixaban'ın 2 doz, rivaroxabanın 1 doz kesilerek yapılması
- ✓ İşlemin YOAK altında yapılması

VKA Kesmeden (terapötik INR altında) ablasyon

- ✓ INR alt sınırda olmalı (2.0-2.5)
- ✓ İlk heparin bolusu düşük olmalı (80 IU/kg)
- ✓ Hedef ACT aynı (>350-400 sn)
- ✓ Hedef ACT 'ye daha kolay ulaşılıyor
- ✓ Stroke riskini azaltabilir
- ✓ Major kanama riski artmamaktadır
- ✓ Gerekli durumlarda kardiyak tamponad tedavisi güvenli
- ✓ Taze donmuş plazma veya faktör IX hazır olmalı

Antikoagülasyon köprülemede algoritma



Rechenmacher S.J, et al. J Am Coll Cardiol 2015

İşlemin Warfarinin altında yapılması
Köprüleme (bridging)

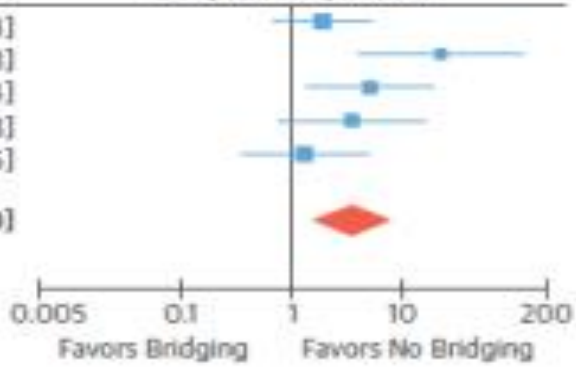
- ✓ VKA 3-4 hafta önce başlanır
- ✓ VKA işlemden 3-4 gün önce kesilir
- ✓ Enoxaparin 0,5-1 mg/kg başlanır
- ✓ Enoxaparin işlemden 12 saat önce kesilir
- ✓ İşlemde iv heparin kullanılır
- ✓ İşlem sonunda protamin
- ✓ İşlemden sonra ACT<250 olunca sheathler çekilir
- ✓ Sheathler çekildikten sonra coumadine + enoxaparine başlanır
- ✓ INR>2 olunca enoxaparine kesilir

Köprülemede major kanama ve tromboembolik olay odds ratios

A Major Bleeding

Study or Subgroup	Bridging Events	Bridging Total	No Bridging Events	No Bridging Total	Weight	Odds Ratio M-H, Random, 95% CI
Daniels et al., 2009	15	342	5	213	24.9%	1.91 [0.68, 5.33]
Garcia et al., 2008	4	108	2	1185	15.3%	22.75 [4.12, 125.68]
Jaffer et al., 2010	13	229	3	263	21.0%	5.22 [1.47, 18.54]
McBane et al., 2010	14	514	2	261	17.9%	3.63 [0.82, 16.08]
Wysokinski et al., 2008	6	204	4	182	20.8%	1.35 [0.37, 4.86]
Total (95% CI)		**1397**		**2104**	**100.0%**	**3.60 [1.52, 8.50]**
Total events	52		16			

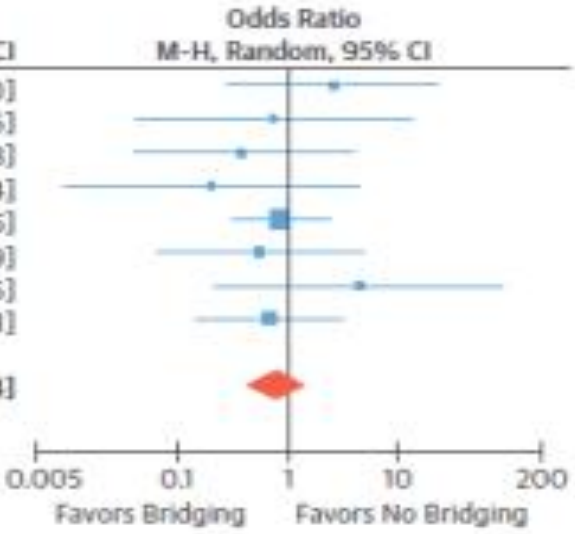
Heterogeneity: $Tau^2 = 0.50$; $Chi^2 = 8.41$, df = 4 (P = 0.08); $I^2 = 52\%$
Test for overall effect: Z = 2.92 (P = 0.004)



B Thromboembolic Events

Study or Subgroup	Bridging Events	Bridging Total	No Bridging Events	No Bridging Total	Weight	Odds Ratio M-H, Random, 95% CI
Daniels et al., 2009	4	342	1	213	8.8%	2.51 [0.28, 22.60]
Garcia et al., 2008	0	108	7	1185	5.2%	0.72 [0.04, 12.76]
Jaffer et al., 2010	1	229	3	263	8.2%	0.38 [0.04, 3.68]
Marquie et al., 2006	0	114	2	114	4.6%	0.20 [0.01, 4.14]
McBane et al., 2010	10	514	6	261	40.5%	0.84 [0.30, 2.35]
Tompkins et al., 2010	1	155	6	513	9.4%	0.55 [0.07, 4.59]
Varkarakis et al., 2005	0	25	3	762	4.7%	4.25 [0.21, 84.56]
Wysokinski et al., 2008	3	204	4	182	18.6%	0.66 [0.15, 3.01]
Total (95% CI)		**1691**		**3493**	**100.0%**	**0.80 [0.42, 1.54]**
Total events	19		32			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.68$, df = 7 (P = 0.82); $I^2 = 0\%$
Test for overall effect: Z = 0.67 (P = 0.50)



Forest plot for major bleeding from Siegal et al. (10) demonstrates a significant odds ratio of 3.6 for patients receiving bridging anticoagulation **(A)**. There is no significant difference in thromboembolic events between bridging and nonbridging **(B)**. CI = confidence interval; M-H = Mantel-Haenszel. Reprinted with permission from Siegal et al. (10).

Yeni Oral Antikoagülan Ajanlar

AF ablasyonu öncesinde/sonrasında VKA iyi bir alternatif!

- ✓ Kanama riski ve emboli riski VKA benzer
- ✓ Daha kolay kullanım
- ✓ Kısa yarım ömürleri nedeniyle ablasyondan sadece 1 gün önce kesilebilirler
- ✓ Etkileri hızlı başladığı için ablasyondan hemen sonra başlanabilirler
- ✓ En az 2-3 ay devam edilir. Bu süreden sonra tedavinin devamı için CHA2DS2-VASc skoruna göre karar verilmelidir

A Prospective Randomized Trial of Apixaban Dosing During Atrial Fibrillation Ablation The AEIOU Trial

Matthew R. Reynolds, J. Scott Allison, Andrea Natale, Ian L. Weisberg, et.al

- **Objectives** This study sought to determine whether uninterrupted apixaban would have similar rates of bleeding and thromboembolic events as does minimally interrupted apixaban at the time of atrial fibrillation (AF) ablation and to compare those results with rates in historical patients treated with uninterrupted warfarin.
- **Background** The safety, efficacy, and optimal dosing regimen for apixaban at the time of AF ablation are uncertain.
- **Methods** This prospective, multicenter clinical trial enrolled 306 patients undergoing catheter ablation for nonvalvular AF and randomized 300 to uninterrupted versus minimally interrupted (holding 1 dose) periprocedural apixaban. A retrospective cohort of patients treated with uninterrupted warfarin at the same centers was matched to the apixaban-treated subjects for comparison. Endpoints included clinically significant bleeding, major bleeding, and nonhemorrhagic stroke or systemic embolism (SE) from the time of ablation through 30 days.
- **Results** There were no stroke or SE events. Clinically significant bleeding occurred in 11.3% of 150 evaluable patients on uninterrupted apixaban and 9.7% of 145 evaluable patients on interrupted apixaban (risk difference: 1.7% [95% confidence interval: −5.5% to 8.8%]; p = NS). Rates of major bleeding were 1.3% with uninterrupted apixaban, and 2.1% with interrupted (risk difference: −0.7%; p = NS). The rates of clinically significant and major bleeding were similar for all apixaban patients combined (10.5% and 1.7%), compared with the matched warfarin group (9.8% and 1.4%).
- **Conclusions** Both uninterrupted and minimally interrupted apixaban at the time of AF ablation were associated with a very low rate of thromboembolic events, and rates of both major (<2%) and clinically significant bleeding were similar to uninterrupted warfarin. (Apixaban Evaluation of Interrupted Or Uninterrupted Anticoagulation for Ablation of Atrial Fibrillation [AEIOU]; NCT02608099)

JACC: Clinical Electrophysiology
DOI: 10.1016/j.jacep.2017.11.005

- ✓FDA elektif invaziv yada cerrahi girişimden önce apiksabanın
  - Kanama riski açısından orta yada yüksek riskli hastalarda 48 saat öncesinden

kesilmesini önermektedir.

Feasibility and Safety of Uninterrupted Rivaroxaban for Periprocedural Anticoagulation in Patients Undergoing Radiofrequency Ablation for Atrial Fibrillation

Results From a Multicenter Prospective Registry

Objectives The purpose of this study was to evaluate the feasibility and safety of uninterrupted rivaroxaban therapy during atrial fibrillation (AF) ablation.

Background Optimal periprocedural anticoagulation strategy is essential for minimizing bleeding and thromboembolic complications during and after AF ablation. The safety and efficacy of uninterrupted rivaroxaban therapy as a periprocedural anticoagulant for AF ablation are unknown.

Methods We performed a multicenter, observational, prospective study of a registry of patients undergoing AF ablation in 8 centers in North America. Patients taking uninterrupted periprocedural rivaroxaban were matched by age, sex, and type of AF with an equal number of patients taking uninterrupted warfarin therapy who were undergoing AF ablation during the same period.

Results A total of 642 patients were included in the study, with 321 in each group. Mean age was 63 ± 10 years, with 442 (69%) males and 328 (51%) patients with paroxysmal AF equally distributed between the 2 groups. Patients in the warfarin group had a slightly higher mean HAS- BLED (hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile international normalized ratio, elderly, drugs/alcohol concomitantly) score (1.70 ± 1.0 vs. 1.47 ± 0.9, respectively; $p = 0.032$). Bleeding and embolic complications occurred in 47 (7.3%) and 2 (0.3%) patients (both had transient ischemic attacks) respectively. There were no differences in the number of major bleeding complications (5 [1.6%] vs. 7 [1.9%], respectively; $p = 0.772$), minor bleeding complications (16 [5.0%] vs. 19 [5.9%], respectively; $p = 0.602$), or embolic complications (1 [0.3%] vs. 1 [0.3%], respectively; $p = 1.0$) between the rivaroxaban and warfarin groups in the first 30 days.

Conclusions Uninterrupted rivaroxaban therapy appears to be as safe and efficacious in preventing bleeding and thromboembolic events in patients undergoing AF ablation as uninterrupted warfarin therapy.

(J Am Coll Cardiol 2014;63:982–8)

Feasibility and Safety of Dabigatran Versus Warfarin for Periprocedural Anticoagulation in Patients Undergoing Radiofrequency Ablation for Atrial Fibrillation

Results From a Multicenter Prospective Registry

Objectives The purpose of this study was to evaluate the feasibility and safety of periprocedural dabigatran during atrial fibrillation (AF) ablation.

Background AF ablation requires optimal periprocedural anticoagulation for minimizing bleeding and thromboembolic complications. The safety and efficacy of dabigatran as a periprocedural anticoagulant for AF ablation are unknown.

Methods We performed a multicenter, observational study from a prospective registry including all consecutive patients undergoing AF ablation in 8 high-volume centers in the United States. All patients receiving dabigatran therapy who underwent AF ablation on periprocedural dabigatran, with the dose held on the morning of the procedure, were matched by age, sex, and type of AF with an equal number of patients undergoing AF ablation with uninterrupted warfarin therapy over the same period.

Results A total of 290 patients, including 145 taking periprocedural dabigatran and an equal number of matched patients taking uninterrupted periprocedural warfarin, were included in the study. The mean age was 60 years with 79% being male and 57% having paroxysmal AF. Both groups had a similar $CHADS_2$ score, left atrial size, and left ventricular ejection fraction. Three thromboembolic complications (2.1%) occurred in the dabigatran group compared with none in the warfarin group ($p = 0.25$). The dabigatran group had a significantly higher major bleeding rate (6% vs. 1%; $p = 0.019$), total bleeding rate (14% vs. 6%; $p = 0.031$), and composite of bleeding and thromboembolic complications (16% vs. 6%; $p = 0.009$) compared with the warfarin group. Dabigatran use was confirmed as an independent predictor of bleeding or thromboembolic complications (odds ratio: 2.76, 95% confidence interval: 1.22 to 6.25; $p = 0.01$) on multivariate regression analysis.

Conclusions In patients undergoing AF ablation, periprocedural dabigatran use significantly increases the risk of bleeding or thromboembolic complications compared with uninterrupted warfarin therapy.

(J Am Coll Cardiol 2012;59: 1168–74)

- ✓ FDA invaziv yada cerrahi girişimden önce dabigatranın

Dabigatran

- **150 mg 2x1 30 gün RFA öncesi**
- **İşlem sabahı stop**
- **Hemostasisden 3 saat sonra tekrar başlanabilir.**

Snipelisky *et al. Heparin dabigatran etkileşimi*

Safety of uninterrupted periprocedural Edoxaban versus Phenprocoumon for Patients undergoing Left Atrial Catheter Ablation Procedures

Abstract

Data about the safety of edoxaban in patients undergoing left atrial (LA) radiofrequency (RF) ablation procedures are lacking. This study sought to compare safety of uninterrupted edoxaban with uninterrupted phenprocoumon administration during LA RF ablation for atrial fibrillation (AF) and atrial tachycardia (AT). In total, 231 patients (mean age: 64 +/- 11years, male 71%) who underwent LA RF ablation under continuous oral anticoagulation (OAC) with edoxaban or phenprocoumon were included in the study. Patients on uninterrupted edoxaban (60mg or 30mg daily for at least 4 weeks) were matched for sex, age and type of arrhythmia with two patients on uninterrupted phenprocoumon (international normalised ratio: 2–3). We identified 77 consecutive patients on edoxaban and n=154 patients on phenprocoumon. Heparin was administered periprocedurally to achieve an activated clotting time (ACT) of 280–300 seconds. No protamine was administered periprocedurally. The primary endpoint was a composite of bleeding, thromboembolic events and death. The primary endpoint was met in 9 patients of the edoxaban group and 22 patients of the phenprocoumon group (P=0.69). No patient in either group died or had a thromboembolic. A major bleeding complication was observed in no patient of the edoxaban group and in 1 patient of the phenprocoumon group (P=>0.99). Minor bleeding complications occurred in 9 patients (12%) of the edoxaban group and in 21 patients (14%) of the phenprocoumon group (*P*=0.84). Uninterrupted OAC with edoxaban appeared to be as safe as uninterrupted OAC with phenprocoumon in patients undergoing LA RF ablation procedures.

DOI: https://doi.org/10.1016/j.amjcard.2017.11.015

An Updated Meta-Analysis of Novel Oral Anticoagulants versus Vitamin K Antagonists for Uninterrupted Anticoagulation in Atrial Fibrillation Catheter Ablation

R. Cardoso, L. Knijnik, A Bhonsale, G Nasi, M Rivera, V Blumer, H Calkins

	Study design	Centers	Patients NOAC/VKA	PAF, % NOAC/VKA	Male, % NOAC/VKA	Age, years† NOAC/VKA	CHA_2DS_2VASc† NOAC/VKA	HAS-BLED† NOAC/VKA	Pre-procedure OAC (days)	Standard NOAC dose	Target ACT	Follow-up
Di Biase[24]	Non-RCT‡	4; US, Eur	200/200	16/16	71/71	65/65	2.28/2.30	1.74/1.74	30	A 5mg BID	>300	30 days
Dillier[17]	Non-RCT‡	1; Eur	272/272	49/46	68/68	62/63	1.8/2.0	NA	30	R 20mg QD	270-300	In-hospital
Konduru[20]	Non-RCT	1; US	11/52	79/55	79/67	56/60	NA	NA	NA	D, dose NA	>350	NA
Kuwahara[11]	RCT	3; JPN	100/100	59/60	75/72	65/66	2.1/2.4	NA	30	A 5mg BID	>300	7 days
Lakkireddy[22]	Non-RCT‡	8; NAmer	321/321	51/51	69/69	63/63	2.17/2.21	1.47/1.70	30	R 20mg QD	300-400	30 days
Maddox[23]	Non-RCT	1; US	212/251	63/57	76/67	62/62	1.73/1.69	NA	30	D 150mg BID	>350-400	In-hospital
Nagao[18]	Non-RCT	1; JPN	D:239 R:102 A:158 VKA:370	D:71 R:79 A:78 VKA:73	D:79 R:69 A:69 VKA:74	D:59 R:61 A:61 VKA:61	D:1.4 R:1.8 A:1.5 VKA:1.5	D:0.8 R:1.1 A:0.9 VKA:0.9	30	D 150mg BID R 15mg QD A 5mg BID	300-350	30 days
RE-CIRCUIT[10]	RCT	104; JPN, Eur RUS, NAmer	317/318	67/68	72/77	59/59	2.0/2.2	NA	30 to 60	D 150mg BID	>300	8 weeks
Shah[25]	Non-RCT	2; US	317/310	75/62	65/55	63/66	2.1/2.8	NA	28	A 5mg BID	>300	90 days
Tao[12]	Non-RCT	1; JPN	76/71	72/77	74/66	66/66	2.2/2.5	1.4/1.5	30	R 15mg QD	>300	30 days
VENTURE-AF[19]	RCT	46; US	124/124	76/70	69/72	76/70	1.5/1.7	NA	21§	R 20mg QD	300-400	30 days
Yoshimura[13]	Non-RCT	1; JPN	55/69	60/50.7	81/75	59/60	1.7/1.5	1.4/1.1	NA	R, dose NA	>300	10 days

An Updated Meta-Analysis of Novel Oral Anticoagulants versus Vitamin K Antagonists for Uninterrupted Anticoagulation in Atrial Fibrillation Catheter Ablation

R. Cardoso, L. Knijnik, A Bhonsale, G Nasi, M Rivera, V Blumer, H Calkins.

Figure 3A. The incidence of major bleeding was significantly lower in the NOAC group (p<0.01).

Study or Subgroup	NOAC Events	NOAC Total	VKA Events	VKA Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Di Biase 2015	2	200	1	200	2.4%	2.00 [0.18, 21.88]
Dillier 2014	1	272	1	272	2.4%	1.00 [0.06, 15.91]
Kuwahara 2016	1	100	0	100	1.2%	3.00 [0.12, 72.77]
Lakkireddy 2014	5	321	7	321	16.7%	0.71 [0.23, 2.23]
Maddox 2013	1	212	3	251	6.6%	0.39 [0.04, 3.77]
Nagao 2015	5	499	4	370	11.0%	0.93 [0.25, 3.43]
RE-CIRCUIT 2017	5	317	22	318	52.5%	0.23 [0.09, 0.59]
Tao 2017	0	76	1	71	3.7%	0.31 [0.01, 7.53]
VENTURE-AF 2015	0	123	1	121	3.6%	0.33 [0.01, 7.97]
Total (95% CI)		**2120**		**2024**	**100.0%**	**0.50 [0.30, 0.84]**
Total events	20		40			

Heterogeneity: Chi² = 6.76, df = 8 (P = 0.56); I² = 0%
Test for overall effect: Z = 2.63 (P = 0.009)

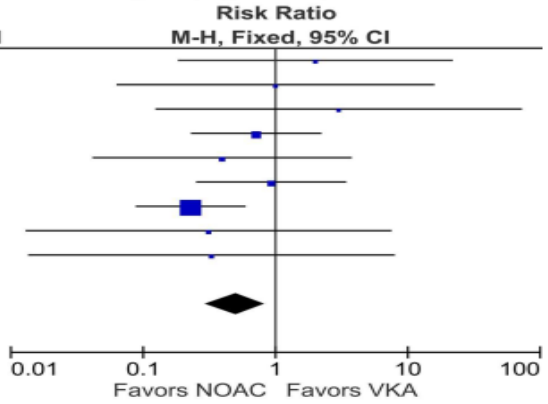
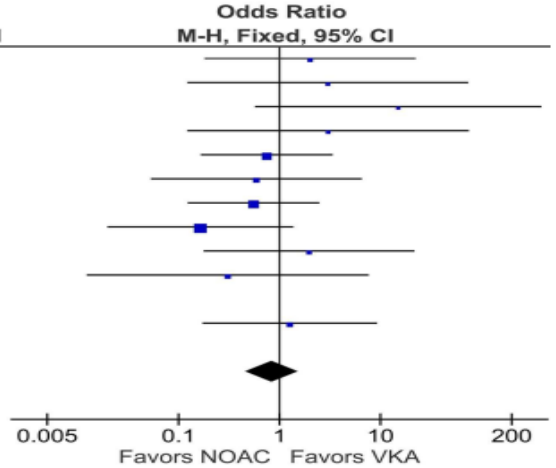


Figure 3B. The incidence of pericardial tamponade was not significantly different between groups (p=0.63).

Study or Subgroup	NOAC Events	NOAC Total	VKA Events	VKA Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Di Biase 2015	2	200	1	200	4.4%	2.01 [0.18, 22.35]
Dillier 2014	1	272	0	272	2.2%	3.01 [0.12, 74.24]
Konduru 2012	1	11	0	52	0.7%	15.00 [0.57, 394.07]
Kuwahara 2016	1	100	0	100	2.2%	3.03 [0.12, 75.28]
Lakkireddy 2014	3	321	4	321	17.4%	0.75 [0.17, 3.37]
Maddox 2013	1	212	2	251	8.0%	0.59 [0.05, 6.55]
Nagao 2015	3	499	4	370	20.1%	0.55 [0.12, 2.49]
RE-CIRCUIT 2017	1	317	6	318	26.3%	0.16 [0.02, 1.37]
Shah 2017	2	317	1	310	4.4%	1.96 [0.18, 21.75]
Tao 2017	0	76	1	71	6.8%	0.31 [0.01, 7.66]
VENTURE-AF 2015	0	124	0	124		Not estimable
Yoshimura 2017	2	55	2	69	7.5%	1.26 [0.17, 9.27]
Total (95% CI)		**2504**		**2458**	**100.0%**	**0.86 [0.47, 1.58]**
Total events	17		21			

Heterogeneity: Chi² = 8.37, df = 10 (P = 0.59); I² = 0%
Test for overall effect: Z = 0.49 (P = 0.63)



Systematic Review/Meta-analysis
Uninterrupted New Oral Anticoagulants Compared With Uninterrupted Vitamin K Antagonists in Ablation of Atrial Fibrillation: A Meta-analysis

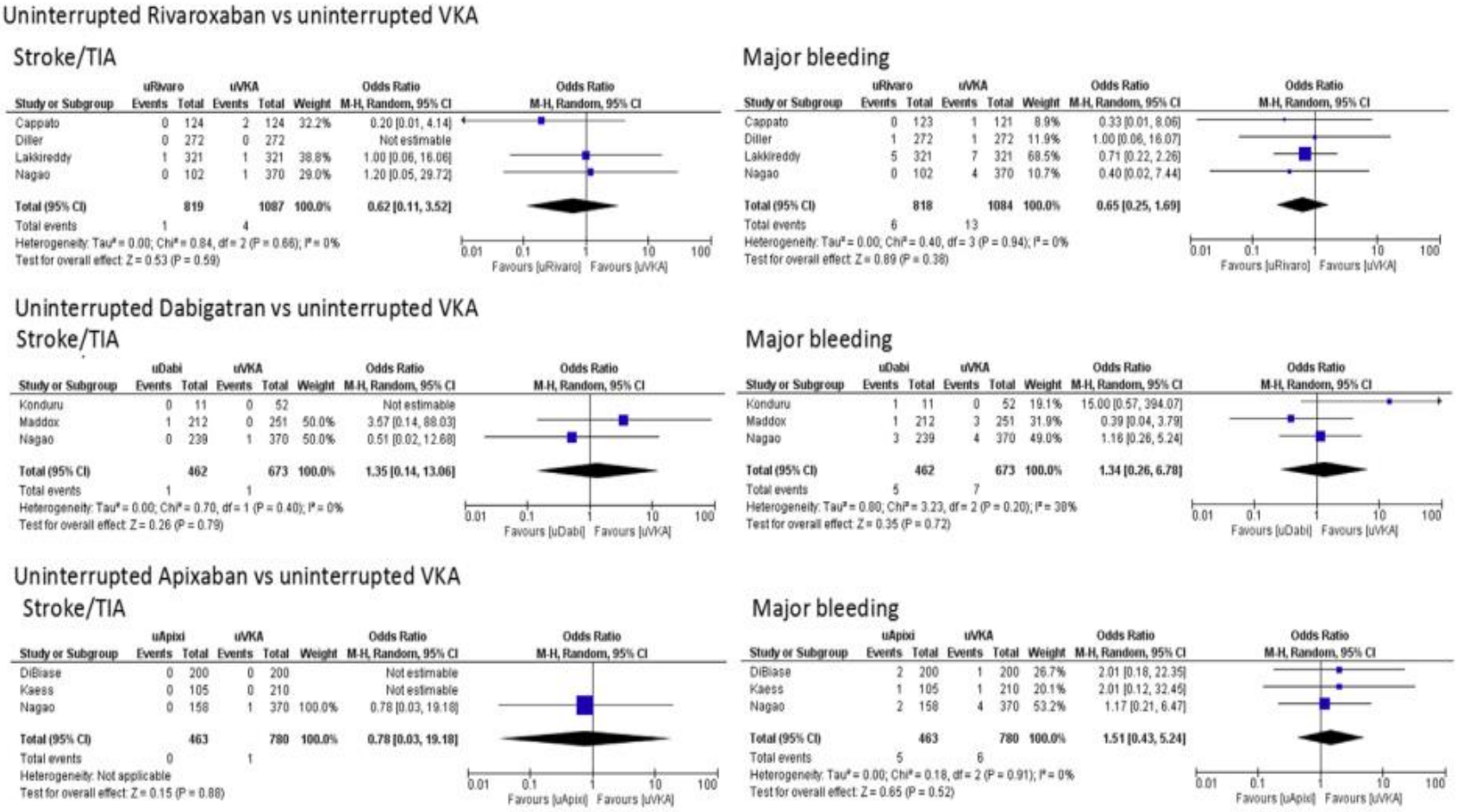


Figure 4. Sensitivity analysis of primary outcome of interest: stroke and major bleeding.

AF Ablasyonu Sırasında Antikogülasyon

Antikoagulation – Ablasyon Sırasında

- ✓İşlemden önce hastada tam kan değerleri ve kan grubu bilinmelidir. İşlem sabahı INR ölçülmelidir.
- ✓İşlem sabahı cross-match yapılmış eritrosit ve taze donmuş plazmanın hazır tutulması önerilmektedir
- ✓İşlem sabahı INR >3,5 ise 1-2 ünite taze donmuş plazma verilmesi önerilmektedir.

Antikoagülasyon- Ablasyon Sırasında

- ✓ **Transseptal ponksiyondan hemen önce veya hemen sonra heparin**
- ✓ Bolus (100–140 IU/kg)
- ✓ İnfüzyon (15–18 IU/kg/saat)
- ✓ Gerekirse ilave boluslar
- ✓ Kateterler sol atriyumdan çıkarılınca heparin kesilir
- ✓ Protamin
- ✓ **Hedef ACT >350–400 sn**

Increased anticoagulation intensity reduces thrombus risk during AF ablation

Ren et al, J Cardiovasc electrophysiol 2005

Incidence of ICE detected mobile thrombus
(on sheath/catheter after T/septal)

	ACT 250-300	ACT >300	p
All pts (n=511)	11.2%	2.8%	<0.05
Pts with SEC (n=179)	44.9%	4.6%	<0.0001

İşlem sırasında antikoagülasyon-I

- ✓ İşlemin warfarin ile sistemik antikoagülasyon altında yapılması işlem sırasında (terapötik ACT seviyelerinde) heparin kulllanım ihtiyacını değiştirmez
- ✓ ACT seviyesinin terapötik antikoagülasyon sağlanıncaya kadar 10-15 dk'da bir ; daha sonra 15-30 dk'da bir monitörizasyonu

İşlem sırasında antikoagülasyon-II

- ✓ Yükleme 60 IU/kg (max 4000 IU), 12 IU/kg/h (max 1000 IU/h)
- ✓ Kateter sol atriyuma ilerletildiğinde kılıfın sağ atriyuma çekilmesi
- ✓ Transseptal kılıfdan devamlı heparinize izotonik infüzyonu
- ✓ İşlem sonunda tüm kateterler sol atriyumdan alındığında heparin infüzyonunun kesilmesi
- ✓ ACT ≤200-250 olduğunda kasık kılıflarının çekilmesi veya ablasyonu takiben heparinin etkisini ortadan kaldıran protaminin kullanımı (sınıf IIa)

Calkins et al. HRS/EHRA/ECAS Catheter and Surgical Ablation, Heart Rhythm 2012

Randomized Comparison of aContinuous and Intermittent Heparin Infusion During Catheter Ablation ofAtrial Fibrillation

OBJECTIVES This study tested the hypothesis that continuous heparin infusions would be favorable for maintaining heparin concentrations during radiofrequency catheter ablation (RFCA) of atrial fibrillation (AF).

BACKGROUND Heparin infusions are essential for RFCA of AF. There is a paucity of data on the details for the optimal heparin infusion during RFCA of AF.

METHODS A total of 333 patients undergoing AF ablation were consecutively enrolled and randomized to intermittent or continuous heparin infusion. A heparin bolus of 100 U/kg was injected just prior to transseptal puncture. The heparin concentration necessary to maintain an optimal activated clotting time (ACT) (300 to 400 s) was determined and checked every 30 min during the procedure. The primary endpoint of the study was the frequency of the maintenance of an optimal intraprocedural ACT.

RESULTS The frequency of an optimal ACT in the continuous group was significantly higher than that in the intermittent group (64.0% vs. 57.6%, respectively, $p < 0.01$), whereas the total heparin level was significantly lower in the continuous group (13,162 ± 4,634 U vs. 15,837 ± 5,243 U, respectively, $p < 0.01$). The standard deviation of the ACT was significantly smaller in the continuous group than in the intermittent group (49 ± 30 vs. 33 ± 18, respectively, $p < 0.01$). Ninety-six patients had new oral anticoagulants (NOACs) before the procedure, and an optimal ACT at the first ACT check was less frequent than in patients taking warfarin (12.5% vs. 59.1%, respectively, $p < 0.01$). There were no significant differences in periprocedural bleeding or thromboembolic complications between the groups.

CONCLUSIONS During AF ablation, a continuous heparin infusion was superior to an intermittent heparin infusion for maintaining an optimal ACT range. (Randomized Comparison of Continuous and Intermittent Heparin Infusion During Catheter Ablation of Atrial Fibrillation [COHERE]; NCT01935557) (J Am Coll Cardiol EP 2016;2:319-26)

AF Ablasyonu Sonrasında Antikogülasyon

Antikoagülasyon – Ablasyon sonrası

- ✓ **LMWH**
  - ✓ Ablasyondan 3-4 saat sonra veya sheath ler çekildikten sonra başlanır ve INR ≥2 olana kadar devam edilir
- ✓ **VKA**
  - ✓ Aynı akşam veya ertesi sabah başlanır
  - ✓ En az 3 ay devam edilir (HRS/EHRA/ECAS:2 ay)
  - ✓ Uzun dönem oral antikoagülasyon CHA2DS2-VASc skoruna göre yapılmalıdır

İşlemi Takiben Antikoagülasyon

- ✓ Kasık kılıflarının çekilmesinden sonra 4-6 saat içinde warfarine tekrar başlanır veya işlem warfarin altında yapıldıysa devam edilir
- ✓ Warfarine tekrar başlanan hastalarda LMWH (enoxaparin 0.5-1.0 mg/kg 2x1) veya IV regüler heparin ile INR 2-3 oluncaya kadar köprüleme
- ✓ İşlem sonrası yüksek kanama riski sebebiyle LMWH dozu azaltılabilir (2X0.5mg/kg)
- ✓ Warfarine alternatif olarak direkt trombin inhibitörleri veya faktör Xa inhibitörlerinin başlanması

AF Ablasyon Sonrası Tromboemboli

- ✓ RF enerjisi verilen lezyon tam endotelizasyonuna kadar koagülasyon kaynağı
  - ✓ Tam süresi bilinmemekle beraber 3 ay yeterli bir süre olarak değerlendirilebilir
- ✓ Atriyumların mekanik kontraktilitesini kazanması
  - ✓ Oluşan fibrozis ve yaralanan atriyal dokunun iyileşmesi (3 ay yeterli süre)
- ✓ Atriyal kontraktilitenin taşikardi sonlanmasından sonra azalması (atrial stunning) haftalar veya aylar sürebilir
  - ✓ Atrimi nüks ederse "atrial stunning" uzun sürebilir

Ablasyon Tedavisinde Kanama ile ilgili Yaklaşım

- ✓ Prothrombin complex concentrate (PCC),
- ✓ Factor VII
- ✓ Factor VIII inhibitor bypass activity(FEIBA)

- ✓ Rivaroxaban ve dabigatran.
  ANTİKOAGÜLAN AKTİVİTELERİ düzeltebilir.

Marlu *et al.*

Company	Compound	Mechanism of action	Reversal for:			Status
			Factor Xa inhibitors	Dabigatran	LMWH/ Fondaparinux	
Portola Pharmaceuticals	PRT064445/ (andexanet alfa)	Recombinant factor Xa analogue that binds to direct factor Xa inhibitors and antithrombin	Yes	No	Yes (antithrombin-mediated factor Xa inhibition)	Phase II completed for rivaroxaban (104), apixaban (105) and enoxaparin (120) (ongoing for edoxaban) Phase III started (apixaban [clinicaltrials.gov NCT02207725]/rivaroxaban [clinicaltrials.gov NCT02220725]) (106, 107) or planned (edoxaban)
Boehringer Ingelheim	BI 655075 (idarucizumab)	Antibody fragment that binds specifically to dabigatran	No	Yes	No	Phase I completed (109, 110) Phase III completed (clinicaltrials.gov NCT02104947) (111)
Perosphere, Inc.	PER977 (aripazine)	Small molecule that binds to heparins, fondaparinux and NOACs	Yes	Yes	Yes	Phase I completed (edoxaban) (112)

LMWH, low-molecular-weight heparin; NOAC, non-vitamin K antagonist oral anticoagulant.

Sonuç

- ✓İşlem öncesi TEE
- ✓İşlem gününe kadar en az 3 hafta OAC devam
- ✓İşlem sırasında ACT kontrolü ile heparin
- ✓İşlemin OAK'lar KESİLMEDEN DEVAM EDİLMESİ
- ✓YOAK sheatler çekildikten sonra 6 saat sonra başlanabilir yada Unfraksiyone Heparin ile beraber işlem akşamı
- ✓İşlemden sonra en az 2 ay OAK sonrası CHADS2 skoruna göre

Teşekkür Ederim