

Antibiyotiklerin Kardiyovasküler Yan Etkileri ve Kardiyovasküler İlaçlar İle Etkileşimleri

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KARDİYOLOJİ ABD**

Antibiyotiklerin kardiyovasküler yan etkileri ve kardiyovasküler ilaçlar ile etkileşimi

Var mı acaba

Neler

Hangi antibiyotikler

Sıklığı ve şiddeti

Klinik Yansıması

Nasıl saptarız

Takip

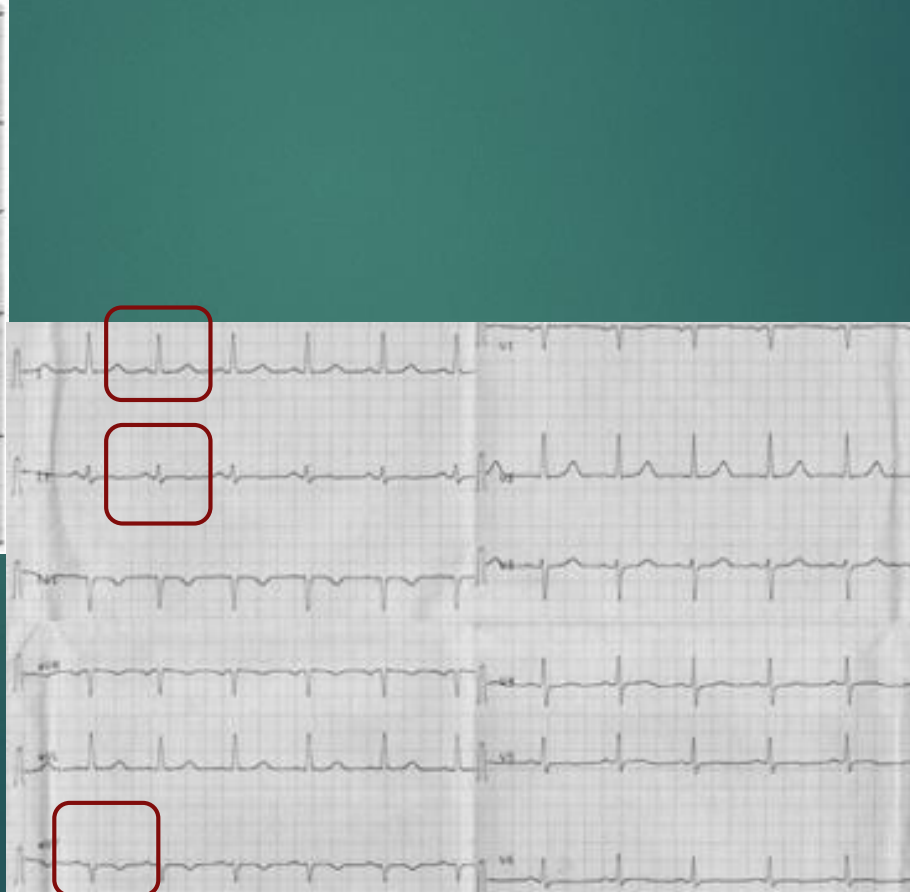
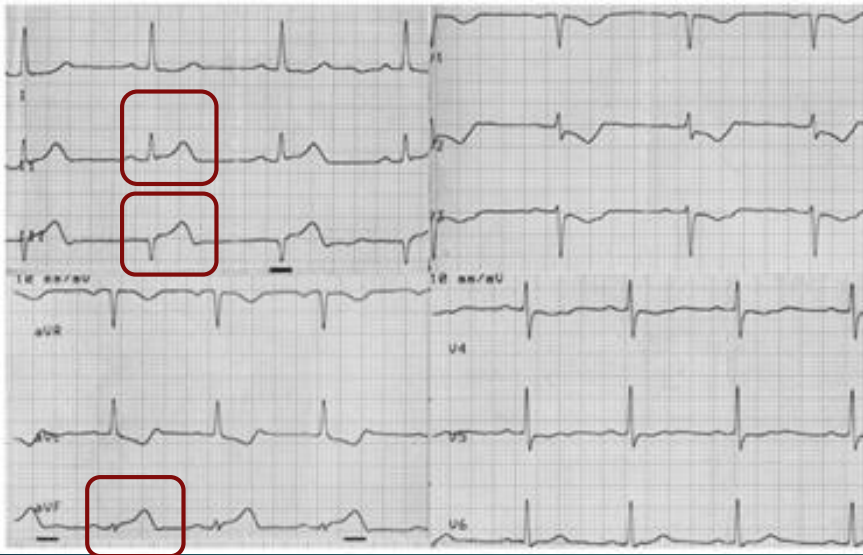
Dikkat edilecek hususlar



Am J Emerg Med. 2012 Oct;30(8):1657.e5-7. doi: 10.1016/j.ajem.2011.08.004. Epub 2011 Nov 17.

ST elevation in inferior derivation, coronary ectasia, and slow coronary flow following ceftriaxone use.

Ilgenli TE¹, Açıklan A, Türkmen S, Avcı A, Akpınar O.



24 yaşında erkek

Alt solunum yolu
enfeksiyonu

Im seftriakson enjeksiyonu

Inferior derivasyonlarda ST
elevasyonu

Seftriaksona bağlı allerjik
reaksiyon

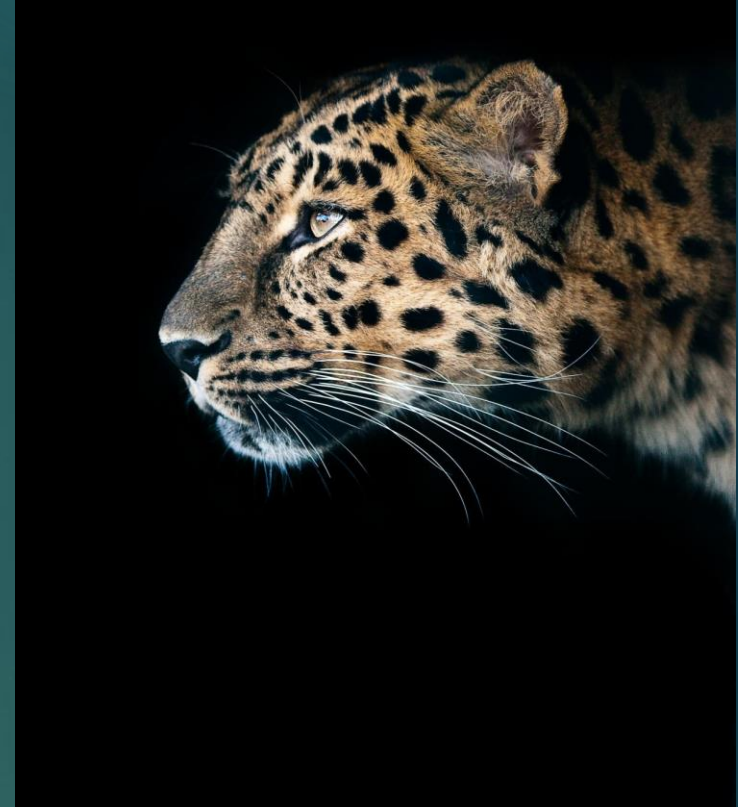
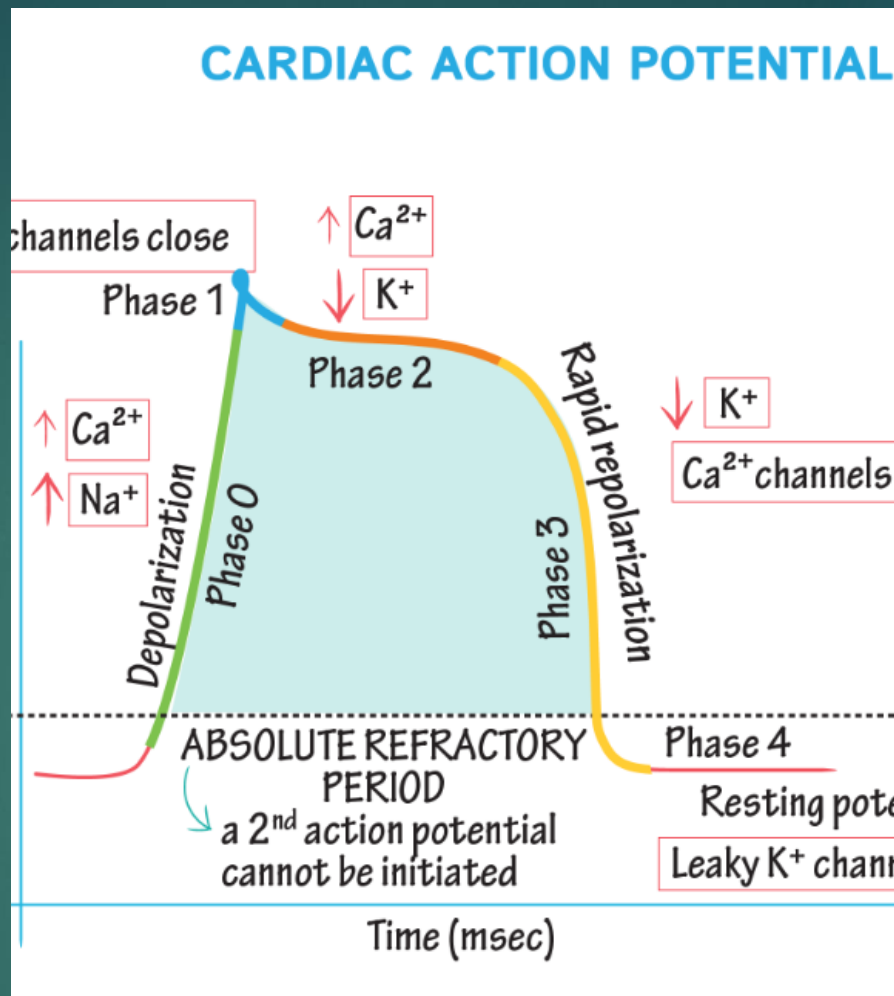
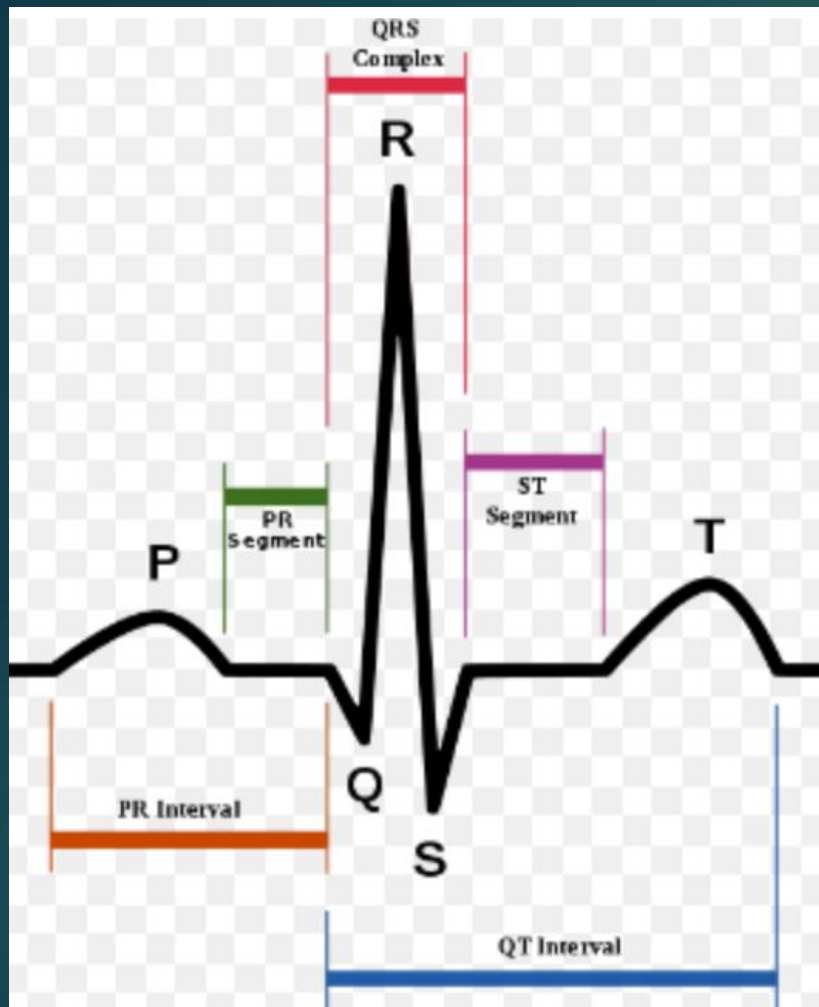
Antibiyotikler ve kardiyovasküler yan etkileri

- ▶ Aritmiler
- ▶ Ani kardiyak ölüm
- ▶ Miyokard infarktüsü
- ▶ Miyokardit
- ▶ Kalp yetersizliği
- ▶ Kardiyomiyopati
- ▶ Aort anevrizması ve diseksiyonu
- ▶





Aritmiler ve QT Mesafesi

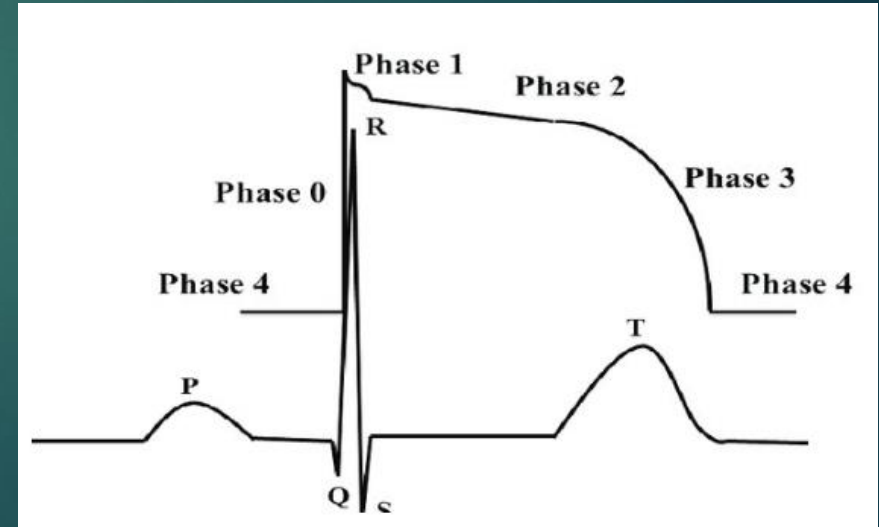
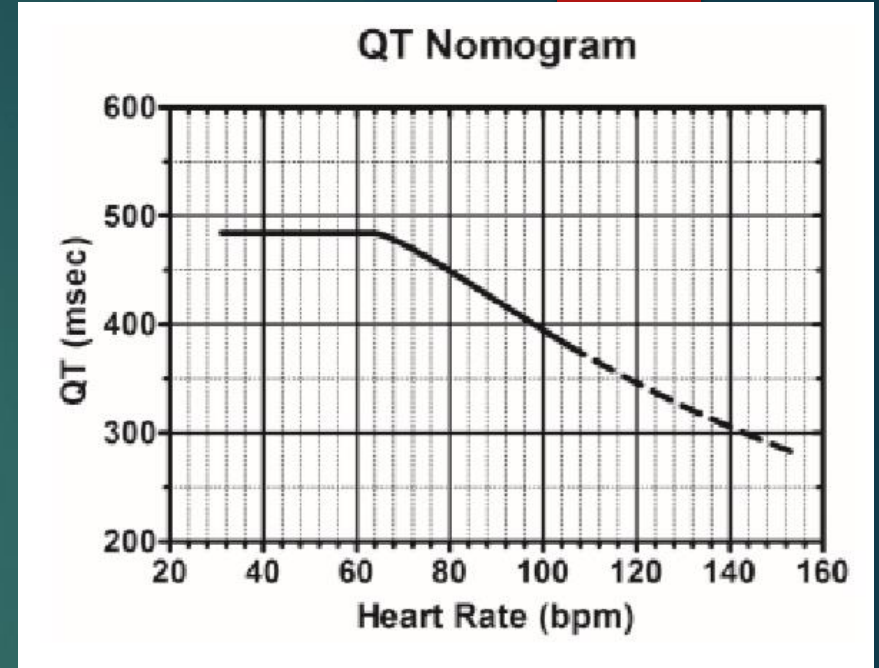


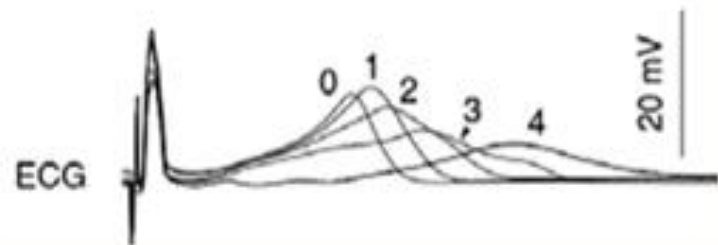
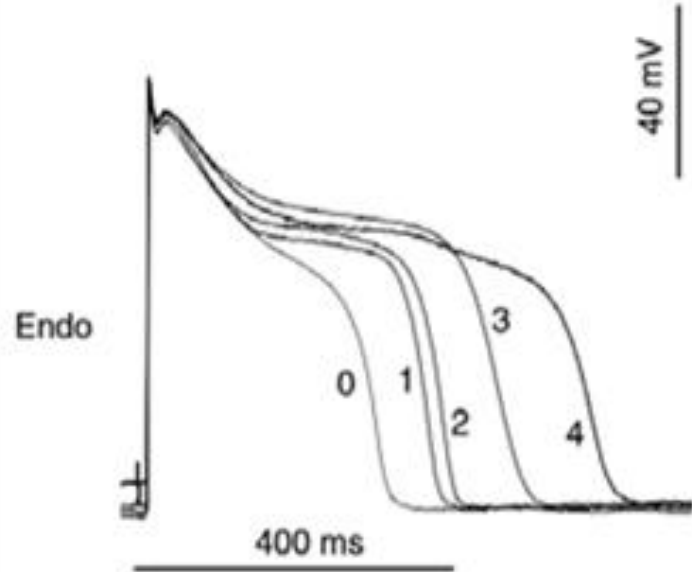
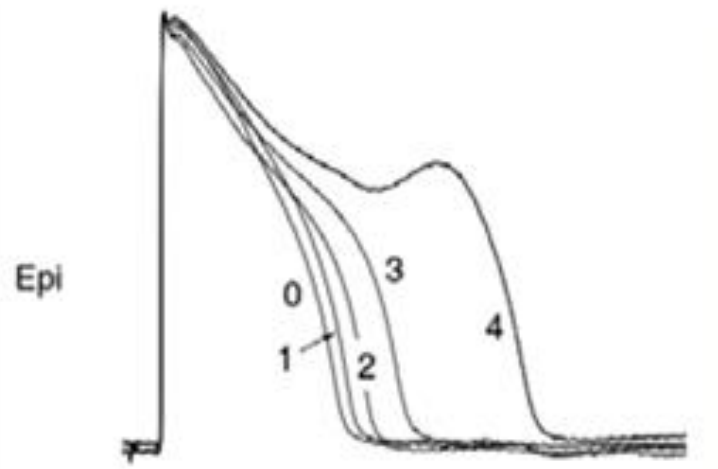
AKSIYON POTANSİYELİ VE EKG

QT MESAFESİ

Correction	Formula
Bazett	$QT_c = QT / \sqrt{RR}$
Fredericia	$QT_c = QT / (RR)^{1/3}$
Framingham	$QT_c = QT + 0.154(1 - RR)$

KALP HIZINA GÖRE DÜZELTİLMİŞ QT
MESAFESİ





Moxifloxacin-induced dispersion of repolarization and EAD.

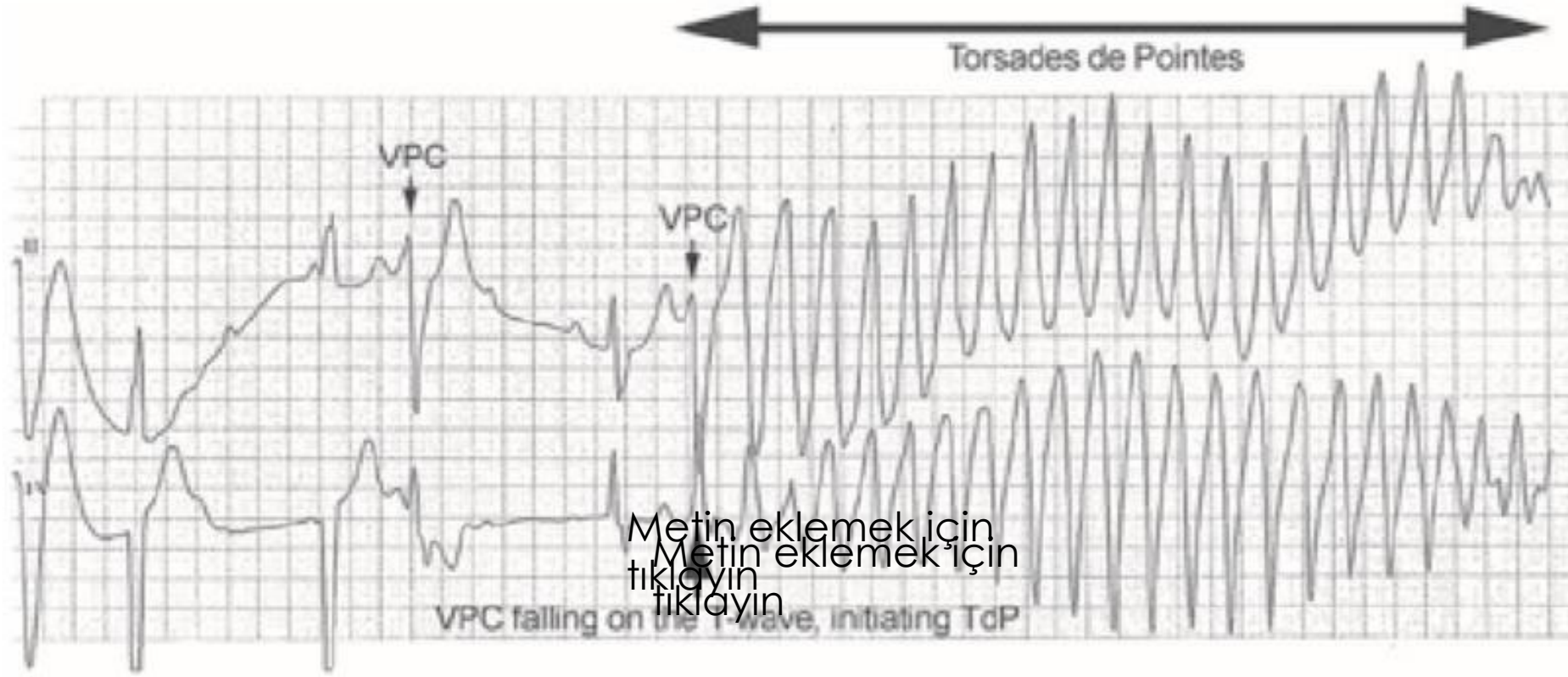
REVIEW

Antibiotic-induced Cardiac Arrhythmias

Elsayed Abo-Salem,¹ John C. Fowler,² Mehran Attari,¹ Craig D. Cox,³ Alejandro Perez-Verdia,⁴ Ragesh Panikkath⁴ & Kenneth Nugent⁴

Cardiovascular
Therapeutics

Cardiovascular Therapeutics 32 (2014) 19–25



Senkop Ani kardiyak ölüm Torsades de pointes(Polimorfik Ventriküler Taşikardi)

Genellikle QT mesafesinin uzaması ile ortaya çıkar.
Kardiyak repolarizasyondaki değişiklik sonucunda meydana gelir.
İlaçlara bağlı uzamada 2 temel mekanizma

- 1.HERG potasyum kanallarındaki blokaj sonucu gelişen aksiyon potansiyelinde repolarizasyon periyodunun uzaması
- 2.Karaciğerde sitokrom P450 üzerine etkide bulunarak diğer proaritmik ilaçların metabolizmasını azaltmak

	Male Patients		Female Patients	
	QT Interval (ms)	Hazard Ratio for Sudden Cardiac Death	QT Interval (ms)	Hazard Ratio for Sudden Cardiac Death
Normal	<430	1.0	<450	1.0
Borderline	431–450	1.3	451–470	1.8
Prolonged	>450	2.5	>470	2.6

55 yaş üzeri hastalarda QT mesafesinin uzaması ve ani kardiyak ölüm riski

Makrolid Grubu Antibiyotikler

- ▶ Vaka takdimlerinde QT uzaması ve torsades de pointes ile ilişkili bulunmuş.
- ▶ İV eritromisin kullanımı artmış aritmi riski
- ▶ 2004 yılında yapılmış geniş ölçekli kohort bir çalışmada eritromisin kullananlarda ani ölüm riski antibiyotik kullanmayanlarla karşılaştırıldığında **2 kat fazla***
- ▶ Eritromisin diğer sitokrom P450 inhibitörleri ile birlikte kullanıldığında ani kardiyak ölüm riskinin **5 kat arttığı** rapor edilmiş**

*Oral erythromycin and the risk of sudden death from cardiac causes. Ray WA, Murray KT, Meredith S: N Engl J Med 2004; 3 51: 1089–1096.

**Immunomodulatory Effects of Macrolide Antibiotics – Part 2 : Respiration 2011;81:75–87 83

Makrolid antibiyotiklerin kullanımı sırasında QT uzaması veya TdP için risk faktörleri

- ▶ Yaş >80
- ▶ Kadın
- ▶ Kalp hastalığı
- ▶ QT uzatan diğer ilaçların kullanımı
- ▶ Azalmış ilaç atılımı
- ▶ Hipokalemi/hipomagnesemi
- ▶ Tedavi öncesi QT mesafesinin uzun olması
- ▶ Bradikardi
- ▶ Genetik yatkınlık

Table 4

Clinical and non-clinical evidences on the activity of macrolides on cardiac repolarisation (proarrhythmic action)

Macrolide	Clinical	Non-clinical
Erythromycin	QT interval prolongation [103–107] Case report of TdP or cardiac arrhythmia [63,108–115]	QT interval prolongation in vivo [78], in vitro [116] Inhibition of cardiac K^+ channel currents (I_{Kr}) in vitro [63–65,117] Blocking of HERG K^+ channel in vitro [61] TdP in vivo [118,119] Review [112,120]
Clarithromycin	Case report of TdP or cardiac arrhythmia [121–127]	QT interval prolongation in vivo [78] Blockade of HERG K^+ channels in vitro [61,67] Review [77]
Roxithromycin	QT interval prolongation [128] Case report of TdP [62]	In vivo arrhythmogenic at dose higher than its clinical range [78] Blockade of HERG K^+ channels in vitro [61]
Azithromycin		In vivo arrhythmogenic at doses higher than those usually prescribed clinically [78]
Spiramycin/acetyl spiramycin	QT interval prolongation [129] Case report of QT interval prolongation [79]	
Josamycin		Blockade of HERG K^+ channels in vitro [61]
Telithromycin	Case report of TdP in post-marketing surveillance [130] QT prolongation in phase III trials [130]	Blockade of I_{Kr} [130] QT prolongation in vitro and in vivo [130]

Klaritromisin

- Klaritromisin ile ilgili 31 Aralık 2018 tarihine kadar yayınlanmış çalışmalar
- Uzun dönem 1 yıl, kısa dönem 3 ay, şu anki 2 hafta
- Bulgularımız, kardiyovasküler hastalıkların komorbiditesine sahip olup olmamasına bakılmaksızın Klaritromisin kullanımını takiben uzun süreli tüm nedenli mortalite arasında anlamlı bir ilişki olmadığını düşündürmüştür.

PLOS ONE

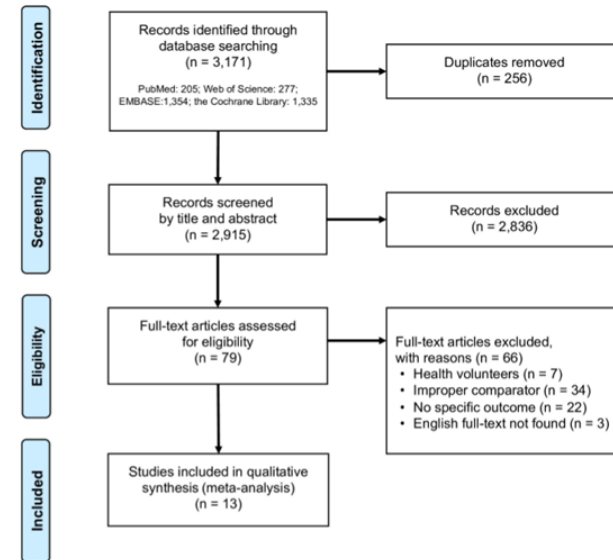
<https://doi.org/10.1371/journal.pone.0226637> December 27, 2019

RESEARCH ARTICLE

Clarithromycin use and the risk of mortality and cardiovascular events: A systematic review and meta-analysis

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Azithromycin and Risk of Cardiovascular Death: A Meta-Analytic Review of Observational Studies

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Abdul H. Qazi, MD,¹ Patricia Erwin, MLS,⁴ Sood Kisra, MD,¹
Abdelrahman Aly, MD,¹ Talha Farid, MD,¹ Mikhael El-Chami, MD,⁵
and Alan P. Wimmer, MD^{1,6}

Azitromisin

Table 1. General characteristics of the included studies.

Author	Study design	Setting	Sample size azithromycin	Country of study	Mean age, yr	Male, %	Indications of therapy	Primary outcome
Khosropour et al ¹⁰	Retrospective cohort study	Data from Oregon Public Health Division	162,385	United States	24	35	STD chlamydia; gonorrhea	All-cause mortality within 10 d of therapy
Rao et al ⁹	Retrospective cohort study	Cohort of US veterans (VA Medical Centers)	594,792	United States	56.8	88	ENT/GU infection, pneumonia, COPD	All-cause mortality with current use (1–5 d) and recent use of azithromycin (6–10 d), arrhythmia
Rey et al ⁸	Retrospective cohort study	Tennessee Medicaid cohort	347,795	United States	48.6	22.5	ENT infections bronchitis	Cardiovascular and all-cause mortality with current (1–5 d) and recent use of azithromycin (6–10 d)
Svanström et al ⁹	Retrospective cohort study	Nationwide historical cohort study	1,102,419	Denmark	39.7	35	Respiratory tract infection, STD, SSTI	Cardiovascular death with current (1–5 d) and recent use of azithromycin (6–10 d), noncardiac death with current azithromycin use (1–5 d)
Mortensen et al ¹¹	Retrospective cohort study	Population based	38,787	United States	77.8	92.8	Pneumonia	30- and 90-d mortality; cardiovascular events within 90 d

COPD, chronic obstructive pulmonary disease; ENT, ear, nose, throat; GU, genitourinary; SSTI, skin and soft tissue infection; STD, sexually transmitted diseases.

Azitromisin

Azitromisin, özellikle daha genç bir popülasyonda, tüm nedenlere bağlı ölümler veya kardiyovasküler ölümlerde anlamlı bir artış ile ilişkili değildir. Bununla birlikte, kardiyovasküler olay riski daha yüksek olan yaşlı hastalar, azitromisin kullanımı ile ilişkili olarak daha yüksek ölüm riski altında olabilir ve muhtemelen bu hastalar için alternatif bir antibiyotik tedavisi düşünülmelidir.

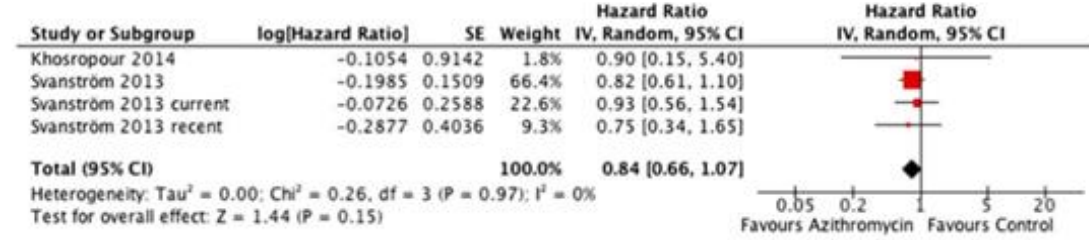


FIGURE 5. Random effects model meta-analysis of risk of death, in the younger population (<40 years), from any cause associated with azithromycin use in comparison with other antibiotics. Error bars indicate the CI.

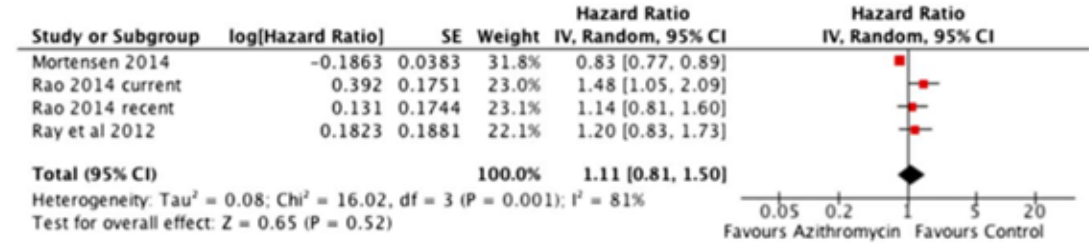


FIGURE 6. Random effects model meta-analysis of risk of death, in the older population (≥ 40 years), from any cause associated with azithromycin use in comparison with other antibiotics. Error bars indicate the CI.



Makrolid antibiyotikler

Makrolidlerden
klaritromisin ve eritromisin
QT uzamasına neden olma
olasılığı daha yüksektir,
en güvenli olanı azitromisindir.

RUIZ AND WORTMANN: CLEVELAND CLINIC JOURNAL OF
MEDICINE VOLUME 86 • NUMBER 4 APRIL 2019 279

Cardiac medications

Antiarrhythmic drugs

Class Ia (Quinidine, Procainamide, Disopromide)

Class III (Dofetilide, Ibutilide, Sotalol)

Non-cardiac medications

Antihistamines (Terfenadine*, Astemizole*)

Antipsychotic and antidepressant agents

Neuroleptic (Haloperidol, Droperidol, Thioridazine, Chlorpromazine)

Atypical antipsychotics (Sertindole*, Ziprasidone, Risperidone, Zimeldine, Citalopram)

Antidepressants (Amitriptyline, Desipramine, Imipramine, Maprotiline, Doxepin, Fluoxetine)

Antibiotics

Quinolone (Sparfloxacin*, Levofloxacin, moxifloxacin, grepafloxacin*)

Macrolide (Erythromycin, Clarithromycin)

Antimalarials (Quinine, halofantrine)

Antiprotozoal (Pentamidine)

Antifungal (Azole group)

Antimotility Agents (Cisapride*)

Methadone

*Withdrawn from market or discontinued

QT Uzamasına
neden olan
bazı ilaçlar



place them in one of three designated categories: Known Risk of TdP (KR), Possible Risk of TdP (PR) or have a Conditional Risk of TdP (CR). The full description of these categories can be found on the CredibleMeds.org website.

Generic Name	Brand Name
Abarelix (PR)	Plenaxis
Abiraterone (CR)	Zytiga and others
Aclarubicin (KR)	Aclacin and others
Alfuzosin (PR)	Uroxatral
Alimemazine (Trimeprazine) (PR)	Nedeltran and others
Amantadine (CR)	Symmetrel and others
Amlodarone (KR)	Cordarone and others
Amisulpride (CR)	Solian and others
Amitriptyline (CR)	Elavil (Discontinued 6/13) and others
Amphotericin B (CR)	Fungilin and others
Amsacrine (Acridinyl aniside) (CR)	Amsidine
Anagrelide (KR)	Agrylin and others
Apalutamide (PR)	Erleada
Apomorphine (PR)	Apokyn and others
Aripiprazole (PR)	Abilify and others
Arsenic trioxide (KR)	Trisenox
Artemether/Lumefantrine (PR)	Coartem
Artemimol/piperaquine (PR)	Eurartesim
Asenapine (PR)	Saphris and others
Astemizole (KR)	Hismanal
Atazanavir (CR)	Reyataz and others
Atomoxetine (PR)	Strattera

Generic Name	Brand Name
Azithromycin (KR)	Zithromax and others
Bedaquiline (PR)	Sirturo
Bendamustine (PR)	Treanda and others
Bendroflumethiazide (Bendrofluazide) (CR)	Aprinox and others
Benperidol (PR)	Anquill and others
Bepidil (KR)	Vascor
Betrixaban (PR)	Bevyxxa
Bortezomib (PR)	Velcade and others
Bosutinib (PR)	Bosulif
Buprenorphine (PR)	Butrans and others
Cabozantinib (PR)	Cometriq
Capecitabine (PR)	Xeloda
Ceritinib (PR)	Zykadia
Chloral hydrate (CR)	Aquachloral and others
Chloroquine (KR)	Aralen
Chlorpromazine (KR)	Thorazine and others
Chlorprothixene (KR)	Truxal
Cilostazol (KR)	Pletal
Cimetidine (CR)	Tagamet
Ciprofloxacin (KR)	Cipro and others
Cisapride (KR)	Propulsid
Citalopram (KR)	Celexa and others

Generic Name	Brand Name
Clarithromycin (KR)	Biaxin and others
Clofazimine (PR)	Lamprene
Clomipramine (CR)	Anafranil
Clotiapine (PR)	Entumine
Clozapine (PR)	Clozaril and others
Cobimetinib (PR)	Cotellic
Cocaine (KR)	Cocaine
Crizotinib (PR)	Xalkori
Cyamemazine (Cyamepromazine) (PR)	Tercian
Dabrafenib (PR)	Tafinlar
Dasatinib (PR)	Sprycel
Degarelix (PR)	Firmagon and others
Delamanid (PR)	Deltiba
Desipramine (PR)	Pertofrane and others
Deutetrabenazine (PR)	Austedo
Dexmedetomidine (PR)	Precedex and others
Dextromethorphan/Quinidine (PR)	Nuedexta
Diphenhydramine (CR)	Benadryl and others
Disopyramide (KR)	Norpace
Dofetilide (KR)	Tikosyn
Dolasetron (PR)	Anzemet
Domperidone (KR)	Motilium and others

QT uzaması
ve/veya TdP
neden olan
ilaçların listesi

Doxepin (CR)	Sinequan and others
Dronedrone (KR)	Multaq
Droperidol (KR)	Inapsine and others
Efavirenz (PR)	Sustiva
Eliglustat (PR)	Cerdelga
Encorafenib (PR)	Braftovi
Entrectinib (PR)	Rozlytrek
Eperisone (CR)	Myonal and others
Epirubicin (PR)	Ellence and others
Eribulin mesylate (PR)	Halaven
Erythromycin (KR)	E.E.S. and others
Escitalopram (KR)	Cipralax and others
Esomeprazole (CR)	Nexium and others
Ezogabine (Retigabine) (PR)	Potiga and others
Famotidine (CR)	Pepcid and others
Felbamate (PR)	Felbatol
Fingolimod (PR)	Gilenya
Flecainide (KR)	Tambocor and others
Fluconazole (KR)	Diffucan and others
Fluorouracil (5-FU) (PR)	Adrucil and others
Fluoxetine (CR)	Prozac and others
Flupentixol (PR)	Depxol and others
Fluvoxamine (CR)	Faverin and others
Furosemide (frusemide) (CR)	Lasix and others
Galantamine (CR)	Reminyl and others
Garenoxacin (CR)	Geninax
Gatifloxacin (KR)	Tequin

Glitteritinib (PR)	Xospata
Glasdegib (PR)	Daurismo
Granisetron (PR)	Kytril and others
Grepafloxacin (KR)	Raxar
Halofantrine (KR)	Halfan
Haloperidol (KR)	Haldol and others
Hydrochlorothiazide (CR)	Apo-Hydro and others
Hydrocodone - ER (PR)	Hysinglaâ,ê ER and others
Hydroquinidine (Dihydroquinidine) (KR)	Serecor
Hydroxychloroquine (KR)	Plaquenil and others
Hydroxyzine (CR)	Atarax and others
Ibogaine (KR)	
Ibutilide (KR)	Convert
Iloperidone (PR)	Fanapt and others
Imipramine (Melipramine) (PR)	Tofranil
Indapamide (CR)	Lozol and others
Inotuzumab ozogamicin (PR)	Besponsa
Isradipine (PR)	Dynacirc
Itraconazole (CR)	Sporanox and others
Ivabradine (CR)	Procoralan and others
Ivosidenib (PR)	Tibsovo
Ketanserin (PR)	Sufrexal
Ketoconazole (CR)	Nizoral and others
Lacidipine (PR)	Lacipil and others
Lansoprazole (CR)	Prevacid
Lapatinib (PR)	Tykerb and others
Lefamulin (PR)	Xenleta

Leuprolide (Leuprorelin) (PR)	Lupron and others
Levofloxacin (KR)	Levaquin and others
Levomopromazine (Methotrimeprazine) (KR)	Nosinan and others
Levomethadone (levamethadone) (PR)	
Levomethadyl acetate (KR)	Orlaam
Levosulpiride (KR)	Lesuride and others
Lithium (PR)	Eskalith and others
Lofexidine (PR)	Lucemyra
Loperamide (CR)	Imodium
Lopinavir/Ritonavir (PR)	Kaletra and others
Maprotiline (PR)	Ludiomil
Melperone (PR)	Bunil and others
Memantine (PR)	Namenda XR
Mesoridazine (KR)	Serentil
Methadone (KR)	Dolophine and others
Metoclopramide (CR)	Reglan and others
Metolazone (CR)	Zytanix and others
Metronidazole (CR)	Flagyl
Mianserin (PR)	Tolvon
Midostaurin (PR)	Rydapt
Mifepristone (PR)	Korlym and others
Mirabegron (PR)	Myrbetriq
Mirtazapine (PR)	Remeron
Moexipril/Hydrochlorothiazide (PR)	Uniretic and others
Moxifloxacin (KR)	Avelox and others
Necitumumab (PR)	Portrazza
Nelfinavir (CR)	Viracept

QT uzaması ve/veya TdP neden olan ilaçların listesi

Generic Name	Brand Name
Nicardipine (PR)	Cardene
Nifekalant (KR)	Shinbit
Nilotinib (PR)	Tasigna
Norfloxacin (PR)	Noroxin and others
Nortriptyline (PR)	Pamelor and others
Nusinersen (PR)	Spinraza
Ofloxacin (PR)	Floxin
Olanzapine (CR)	Zyprexa and others
Omeprazole (CR)	Losec and others
Ondansetron (KR)	Zofran and others
Osimertinib (PR)	Tagrisso
Oxaliplatin (KR)	Eloxatin
Oxytocin (PR)	Pitocin and others
Paliperidone (PR)	Invega and others
Palonosetron (PR)	Aloxi
Panobinostat (PR)	Farydak
Pantoprazole (CR)	Protonix
Papaverine HCl (Intra-coronary) (KR)	
Paroxetine (CR)	Paxil and others
Pasireotide (PR)	Signifor
Pazopanib (PR)	Votrient
Pentamidine (KR)	Pentam
Perflutren lipid microspheres (PR)	Definity and others
Perphenazine (PR)	Trilafon and others
Pilsicainide (PR)	Sunrhythm
Pimavanserin (PR)	Nuplazid
Pimozide (KR)	Orap
Pipamperone (PR)	Dipiperon and others
Piperacillin/Tazobactam (CR)	Tazosyn and others
Pitolisant (Tiprolisant) (PR)	Wakix

Generic Name	Brand Name
Posaconazole (CR)	Noxafil and others
Pretomanid (PR)	
Primaquine phosphate (PR)	
Probucol (KR)	Lorelco
Procainamide (KR)	Pronestyl and others
Promethazine (PR)	Phenergan
Propafenone (CR)	Rythmol SR and others
Propofol (KR)	Diprivan and others
Prothipendyl (PR)	Dominal and others
Quetiapine (CR)	Seroquel
Quinidine (KR)	Quinaglut and others
Quinine sulfate (CR)	Qualaquin
Ranolazine (CR)	Ranexa and others
Ribociclib (PR)	Kisqali
Rilpivirine (PR)	Edurant and others
Risperidone (CR)	Risperdal
Romidepsin (PR)	Istodax
Roxithromycin (KR)	Rulide and others
Saquinavir (PR)	Invirase(combo)
Sertindole (PR)	Serdolect and others
Sertraline (CR)	Zoloft and others
Sevoflurane (KR)	Ultane and others
Siponimod (PR)	Mayzent
Solifenacin (CR)	Vesicare
Sorafenib (PR)	Nexavar
Sotalol (KR)	Betapace and others
Sparfloxacin (KR)	Zagam
Sulpiride (KR)	Dogmatil and others
Sultopride (KR)	Barnetil and others
Sunitinib (PR)	Sutent

Generic Name	Brand Name
Tacrolimus (PR)	Prograf and others
Tamoxifen (PR)	Nolvadex and others
Telaprevir (CR)	Incivo and others
Telavancin (PR)	Vibativ
Telithromycin (PR)	Ketek
Terfenadine (KR)	Seldane
Teripressin (KR)	Teripress and others
Terodiline (KR)	Micturin and others
Tetrabenazine (PR)	Nitoman and others
Thioridazine (KR)	Mellaril and others
Tiaprude (PR)	Tiaprudal and others
Tipiracil/Trifluridine (PR)	Lonsurf
Tizanidine (PR)	Zanaflex and others
Tolterodine (PR)	Detrol and others
Toremifene (PR)	Fareston
Torsemide (Torasemide) (CR)	Demadex and others
Tramadol (PR)	Crispin and others
Trazodone (CR)	Desyrel and others
Trimipramine (PR)	Surmontil and others
Tropisetron (PR)	Navoban and others
Valbenazine (PR)	Ingrezza
Vandetanib (KR)	Caprelsa
Vardenafil (PR)	Levitra
Vemurafenib (PR)	Zelboraf
Venlafaxine (PR)	Effexor and others
Voriconazole (CR)	VFend
Vorinostat (PR)	Zolinza
Ziprasidone (CR)	Geodon and others
Zotepine (PR)	Losizopilon and others
Zuclopenthixol (Zuclopentixol) (PR)	Cisordinol and others

QT uzaması
ve/veya TdP
neden olan
ilaçların listesi

Hastane dışı kardiyak ölümlerde Makrolid antibiyotikler ve Penisilin V

Makrolidlerle tedavi
sırasında hastane dışı
kardiyak ölüm riski
penisilin V'dekine
benzer,
veriler makrolidlerle
ilişkili ek risk olmadığını
düşündürmektedir.

Open Access

Research

BMJ Open Does macrolide use confer risk of out-of-hospital cardiac arrest compared with penicillin V? A Danish national case-crossover and case-time-control study

Frederik Boetius Hertz,¹ Aksel Jensen,^{2,3} Jenny D Knudsen,⁴ Magnus Arpi,¹ Charlotte Andersson,⁵ Gunnar H Gislason,^{5,6,7} Lars Køber,⁸ Christian Torp-Pedersen,⁹ Freddy Lippert,¹⁰ Peter E Weeke¹¹

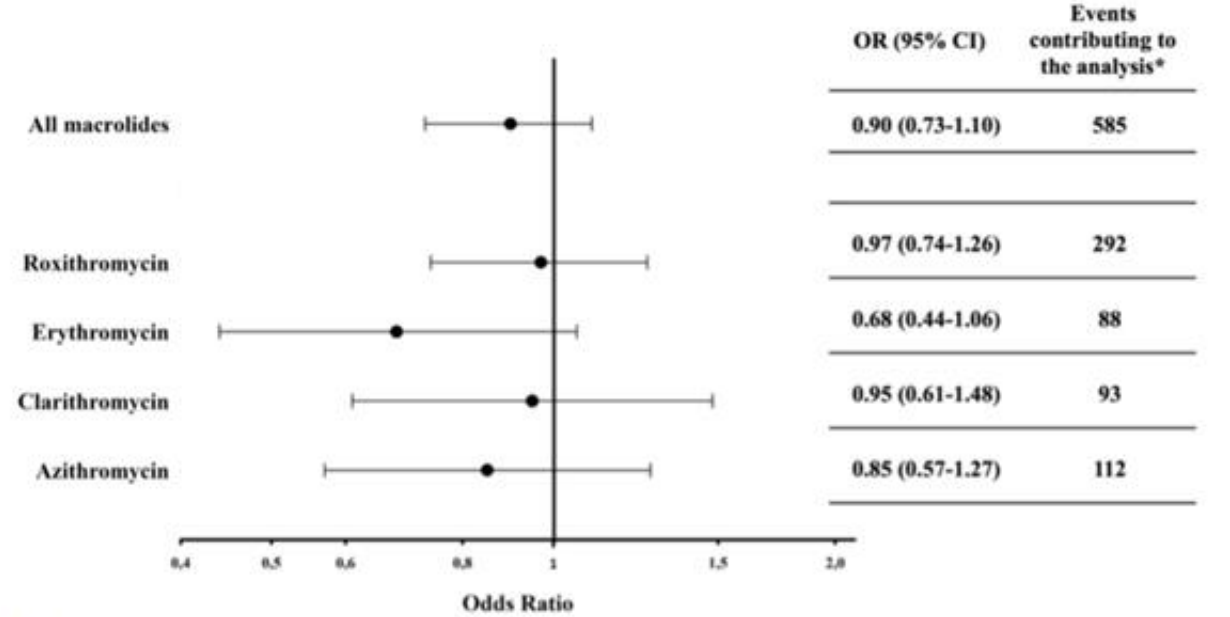


Figure 2 Macrolide treatment and risk of out-of-hospital cardiac arrest using penicillin V as the comparative reference according to the case-crossover analysis. Presented are OR from the conditional logistic regression analysis in case-crossover models (95%CI). *OHCA cases contributing to the analysis were those having a discordant drug exposure history in the case and control periods. OHCA, out-of-hospital cardiac arrest.

Kinolonlar

- ▶ QT uzaması kinolonların bir sınıf etkisidir.
- ▶ Siprofloksasinin kardiyovasküler yan etkiler açısından en güvenli olduğu düşünülmektedir.

RUIZ AND WORTMANN: CLEVELAND CLINIC
JOURNAL OF MEDICINE VOLUME 86 •
NUMBER 4 APRIL 2019 279

REVIEW

MARIA ELENA RUIZ, MD

Section of Infectious Diseases, Department of
Medicine, MedStar Washington Hospital Center,
Washington, DC

GLENN W. WORTMANN, MD

Section of Infectious Diseases, Department of
Medicine, MedStar Washington Hospital Center,
Washington, DC; Professor of Clinical Medicine
(Infectious Diseases), Georgetown University,
Washington, DC

Unusual effects of common antibiotics



Siprofloksasine baęlı TdP Vaka Takdimi

65 yaşı erkek

Üriner sistem enfeksiyonu nedeniyle
siprofloksasin

Nöbet benzeri aktivite

QT mesafesi 7 gün sonra normal seviyelere
geliyor

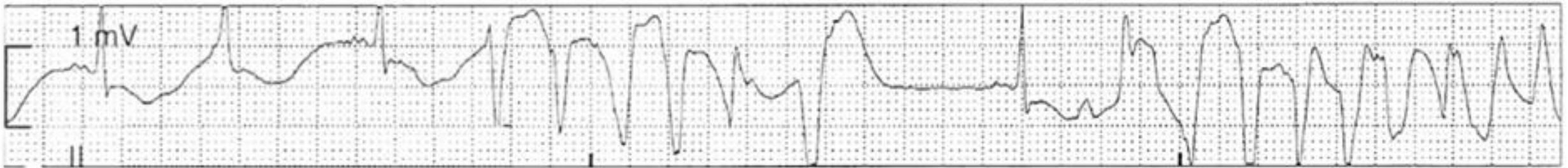


Fig. 2 Telemetry strip during first day of admission showing long QT interval and short runs of TdP.



Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid



The risk of cardiac events in patients who received concomitant levofloxacin and amiodarone[☆]



Luigi Brunetti^{a,b,1}, Seung-Mi Lee^{a,c,1}, Ronald G. Nahass^{a,b}, David Suh^d, Benjamin Miao^a, John Bucek^b, Dongwon Kim^c, Ok-Kyu Kim^c, Dong-Churl Suh^{c,*}

Levofloksasin ve amiadoron birlikte kullanımı

KARDİYAK OLAYLARI (VENTRİKÜLER ARİTMİLER, KARDİYAK AREST VE ÖLÜM) 6 KATDAN FAZLA ARTTIRIYOR.

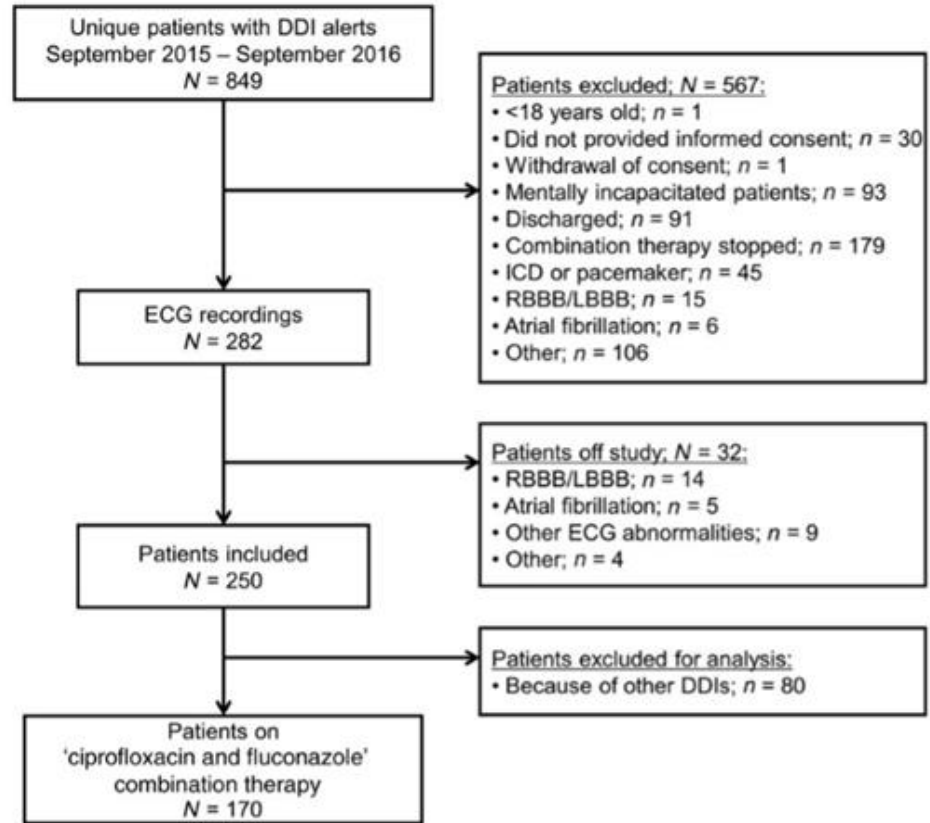
DRUG SAFETY

QTc prolongation during ciprofloxacin and
fluconazole combination therapy: prevalence
and associated risk factors

Correspondence Drs Florine A. Berger, Department of Hospital Pharmacy, Erasmus University Medical Centre, Rotterdam, The Netherlands. Tel.: +31 10 703 3202; Fax: +31 10 703 2400; E-mail: f.berger@erasmusmc.nl

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Florine A. Berger¹, Nico Monadian², Natasja M. S. de Groot³, Bart Santbergen⁴, Heleen van der Sijs¹, Matthijs L. Becker⁵, Annoek E. C. Broers⁶, Teun van Gelder¹ and Patricia M. L. A. van den Bemt¹



Siprofloksasin ve Flukanazol birlikte kullanımı

QTC UZAMASI İLE İLİŞKİLİ HERHANGİ BİR RİSK FAKTÖRÜ BULUNMADI.



PR MESAFESİ VE AV BLOKLAR

Eritromisin ve Verapamil

Kalsiyum kanal blokeri
ve makrolid antibiyotiđi
birlikte kullanan
hastalar PR
mesafesinde uzama ve
AV Blok gelişimi
açasından yakından
monitorize edilmelidir.



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Toxicology and Applied Pharmacology 214 (2006) 24–29

Toxicology
and Applied
Pharmacology

www.elsevier.com/locate/ytap

Erythromycin potentiates PR interval prolonging effect of verapamil in the rat: A pharmacodynamic drug interaction

Yaman Dakhel, Fakhreddin Jamali *

Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, Alberta, Canada T6H 2N8

Received 19 September 2005; revised 3 November 2005; accepted 26 November 2005

Available online 8 February 2006



Concomitant Use of Nifedipine and Clarithromycin Leading to Pulseless, Bradycardic Arrest

American Journal of Therapeutics (2019) 26(4)

Ryan M. D. Cook, PharmD¹
Aileen S. Garcia-Gayoso, MD²
Jennifer D. Twilla, PharmD, BCPS^{1,3}

Nifedipin ve Klaritromisin

72 yaş kadın

Akut bronşit tanısıyla Klaritromisin 500 mg 2x1

Bradikardik arest ve nabızsız elektriksel aktivite gelişmiş

Kardiyopulmoner resüstasyon, epinefrin ve atropin sonrası
spontan dolaşım ve kardiyak ritim geri dönmüş

Amfoterasin B ve AV Blok

9 ay kız

Sistemik fungal enfeksiyon

Tedavinin 3. günü bradikardi atakları
ve 2. derece AV blok

İlacın kesilmesini takiben 8. gün
bradikardi epizodları düzeldi.

Sanches BF, et al. BMJ Case Rep 2014.
doi:10.1136/bcr-2013-202688

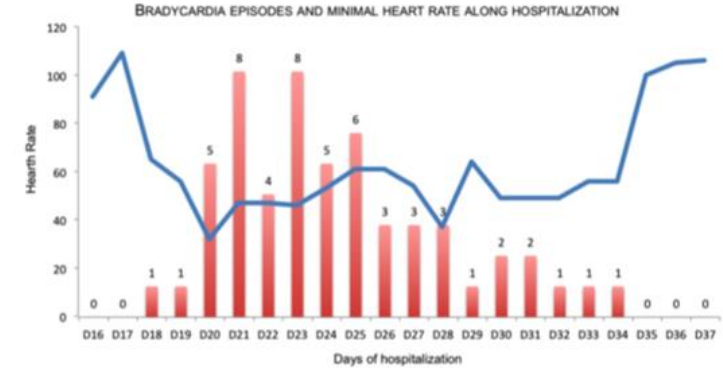
Unexpected outcome (positive or negative) including adverse drug reactions

CASE REPORT

Atrioventricular block related to liposomal amphotericin B

Bruno Fernandes Sanches,¹ Pedro Nunes,² Helena Almeida,² Mónica Rebelo³

Figure 1 Graphic representation of the bradycardia episodes along hospitalisation. The blue line represents the evolution of minimal heart rate value and the red columns represent the number of bradycardia episodes per day since the 16th to the 37th days of hospitalisation (number of the episodes in the top of each column). Amphotericin therapy was started on the 16th day and was suspended on the 27th day of hospitalisation.



MİYOKARD İNFARKTÜSÜ

Makrolid antibiyotikler ve Miyokard İnfarktüsü



AMERICAN
SOCIETY FOR
MICROBIOLOGY

Antimicrobial Agents
and Chemotherapy®

EPIDEMIOLOGY AND SURVEILLANCE



Systematic Review, Meta-analysis, and Network Meta-analysis of the Cardiovascular Safety of Macrolides

Einat Gorelik,^{a,b} Reem Masarwa,^a Amichai Perlman,^a Victoria Rotshild,^a Mordechai Muszkat,^c Ilan Matok^a

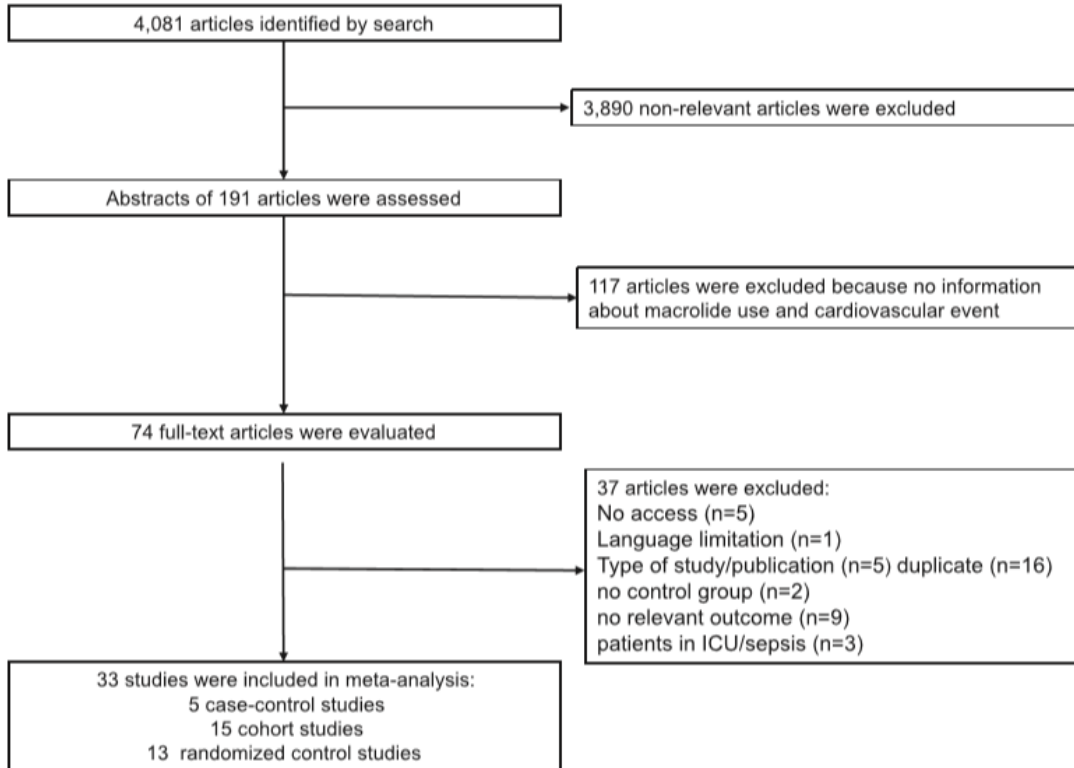


TABLE 1 Treatment ranked by probability of highest risk of MI

Medication	P score ^a
Erythromycin	0.94
Clarithromycin	0.77
Azithromycin	0.31
Nonmacrolide	0.24
Roxithromycin	0.23

^aThe P score is derived from network meta-analysis and represents the mean extent of certainty that a given treatment has greater risk of MI among the included treatments, measured on a scale from 0 (best) to 1 (worst).

13 Randomize, 7 kohort ve 1 vaka kontrol toplam 20 çalışmanın analizinde makrolid antibiyotik tedavisini takiben miyokardial infarktüs riskinde istatistiki olarak anlamlı %15 artış izlenmiştir (OR 1.15 [95% CI, 1.01 to 1.30], P 0.00001)

DİLATE KARDİYOMİYOPATİ VE KALP YETMEZLİĞİ

CAP-START Trial

Toplum kökenli pnömoni tedavisinde beta-laktam monoterapi, beta laktam-makrolid kombine tedavi ve florokinolon monoterapi karşılaştırılması

Kardiyak olay 2017 hastanın 146 sında(%6.9); kalp yetmezliği 101(% 4.8), aritmi 53 (% 2.5), ve miyokard iskemisi 14 (%0.7) (Toplam 207)

Azitromisin 11 (%5.3), Klaritromisin 18(%7.2), eritromisin 31(11.2)

Ciprofloksasin 9(%3.8), Levofloksasin 5(%2.6), Moxifloksasin 23(%4.1)

Florokinolonlar özellikle kalp yetmezliği açısından daha düşük riske sahiptir

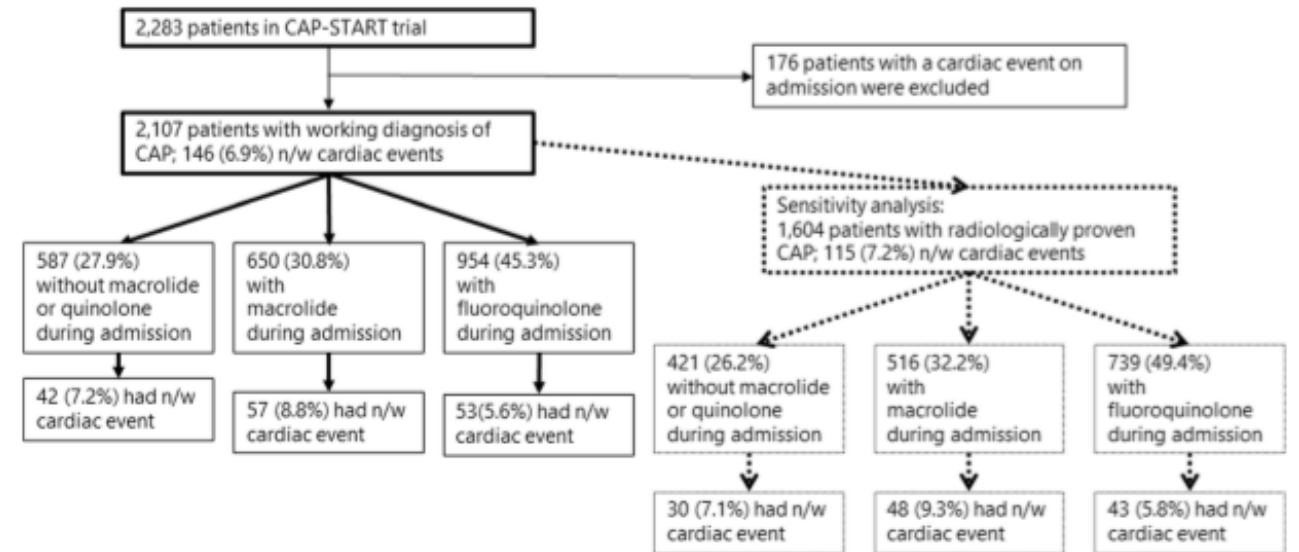
RESEARCH ARTICLE

Open Access



Cardiac events after macrolides or fluoroquinolones in patients hospitalized for community-acquired pneumonia: post-hoc analysis of a cluster-randomized trial

Douwe F. Postma^{1,2,4*}, Cristian Spitoni³, Cornelis H. van Werkhoven¹, Leontine J. R. van Elden⁵, Jan Jelrik Oosterheert⁴ and Marc J. M. Bonten^{1,6}



Cardiac events in original trial arms:					
BL monotherapy	per protocol	29/351 (8%)	FQL monotherapy	per protocol	34/639 (5%)
	macrolide	7/75 (9%)		macrolide	0/42 (0%)
	quinolone	8/139 (6%)		beta-lactam	5/94 (5%)
BLM combination therapy	per protocol	41/458 (9%)			
	beta-lactam	6/121 (5%)			
	quinolone	2/46 (4%)			

Amfoterasin B ve Dilate Kardiyomiyopati



The American Journal of Medicine

Volume 97, Issue 6, December 1994, Pages 560-562



Amphotericin B-induced dilated cardiomyopathy

Edward L. Arsura MD, FACP, Yahya Ismail MD, Sheldon Freedman MD, A.R.S.R., Karunakar MD, FACC

Show more

[https://doi.org/10.1016/0002-9343\(94\)90353-0](https://doi.org/10.1016/0002-9343(94)90353-0)

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Journal of Antimicrobial Chemotherapy (2004) **53**, 115–117

DOI: 10.1093/jac/dkg472

Advance Access publication 4 December 2003

JAC

Reversible dilated cardiomyopathy related to amphotericin B therapy

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Caroline C. DeWitt⁴

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INTERNATIONAL JOURNAL OF
Antimicrobial
Agents

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International Journal of Antimicrobial Agents 25 (2005) 444–447

Reversible dilated cardiomyopathy associated with amphotericin B treatment

Ioannis Moyssakis^a, Theodoros P. Vassilakopoulos^b, Nikolaos V. Sipsas^{c,*},
Alexandros Perakis^a, Alexandra Petrou^b, Nikolaos Kosmas^c, Gerassimos A. Pangalis^b

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^b First Department of Internal Medicine, National and Kapodistrian University of Athens and Laikon General Hospital, Athens, Greece

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Received 19 November 2004; accepted 18 February 2005

Farm Hosp. 2006 Jul-Aug;30(4):260-1.

[Subacute cardiomyopathy and liposomal amphotericin B].

[Article in Spanish]

Quer N, Soy D, Castro P, Nicolás JM.

Amfoterasin B
ve
Dilate Kardiyomiyopati

Case Report

Reversible dilated cardiomyopathy associated with amphotericin B therapy

J. R. Soares* MD, M. C. P. Nunes*† MD PhD, A. F. Leite* MD, E. B. Falqueto* MD, B. E. R. A. Lacerda* MD and T. C. A. Ferrari*† MD PhD

*Hospital das Clínicas of the Universidade Federal de Minas Gerais, Belo Horizonte, MG, and †Department of Internal Medicine, School of Medicine of the Universidade Federal de Minas Gerais, Belo Horizonte, MG, Brazil

45 yaş erkek

Daha önce kardiyak yakınma yok

Visseral leishmaniasis tanısı ile AmB–
deoxycholate, 06 mg/ kg/day, 18 gün
(kümülativ doz, 900 mg).

Tedavi sırasında gözlenen yan etki yok

Tedavinin tamamlanmasından 2 gün önce
ekokardiyografi normal

Taburcu olduktan 5 gün sonra akut kalp
yetmezliği

MIYOKARDİT

Akut Hipersensitivite Miyokarditi

VAKA 1

9 yaş erkek

Sağ bacak sellülit nedeniyle
sefalekssin tedavisi

24 saat sonra sternum arkasında
göğüs ağrısı, nefes darlığı ve
hipotansiyon

3. gün ekokardiyografi lv
dilatasyonu ef düşüklüğü

VAKA 2

5 yaş erkek

Ateş ve öksürük nedeniyle 1 hafta
süre ile sefprozil kullanılmış

2 saat içinde kardiyopulmoner
arrest

Pediatr Cardiol (2006) 27:777-780
DOI 10.1007/s00246-006-1430-0

Fatal Cephalosporin-Induced Acute Hypersensitivity Myocarditis

Kudakwashe R. Chikwava · Van H. Savell Jr ·
Theonia K. Boyd

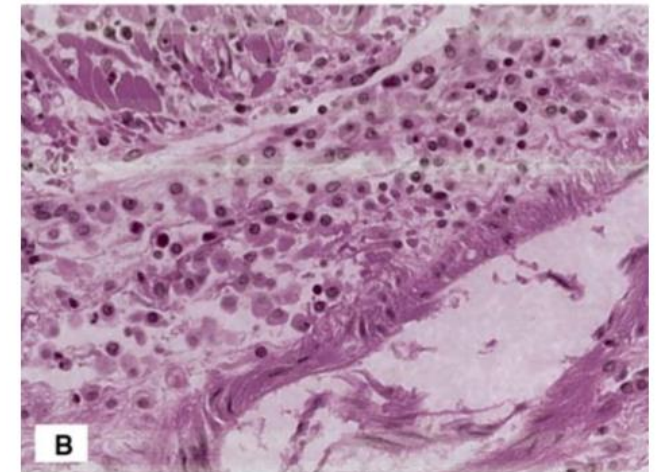
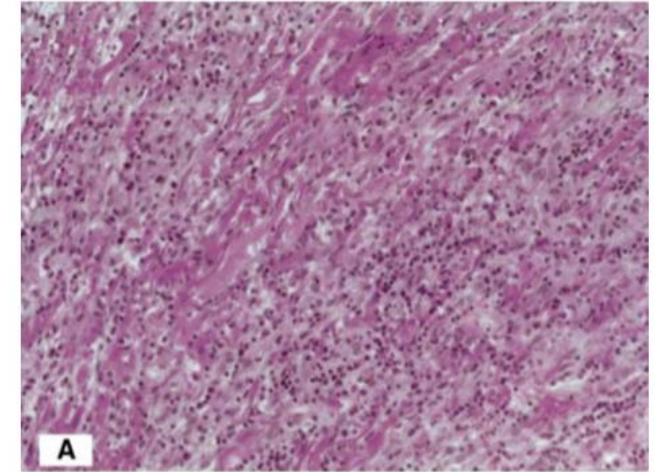


Fig. 1 These photomicrographs of patient 1's heart (H&E, 200×) show myocyte necrosis with extensive eosinophilic inflammatory infiltrate (a) and histiocytic interstitial and perivascular inflammatory cell infiltrate (b)

Sefalosporin kaynaklı akut hipersensitivite miyokarditi



Table 2 Summary of reported cases of acute hypersensitivity myocarditis associated with administration of a cephalosporin

Case no	Implicated drug(s)	History	Outcome
1	Ciprofloxacin	46-year old jockey with a left cholesteatoma status post left cortical mastoidectomy	Died of multiorgan failure including AHM after 5 weeks
2	Cefepime	55-year-old man with a common cold	Improved after discontinuation of the drug along with mechanical assistance involving intraaortic balloon pumping and steroid pulse therapy
3	Cefaclor	12-year-old girl with otitis media	Improved after discontinuation of the drug and inotropic support

Sefalosporin kaynaklı akut hipersensitivite miyokarditi, klinik olarak genellikle şüphelenilmeyen nadir fakat potansiyel olarak ölümcül bir durumdur.

Sistemik viral bir hastalığı, viral miyokarditi veya sepsisi taklit edebilen semptomlarla başvuran hastalarda hastalık bilgisi kritik öneme sahiptir. Erken şüphelenildiğinde antibiyotiğin kesilmesi ve terapötik immünsüpresyon hayat kurtarıcı olabilir.

Penisilin kaynaklı Fulminan Miyokardit

11 yaş kız

3 gündür olan ateş, boğaz ağrısı,
halsizlik

Im penisilin

1 saat sonra akut kızarıklık, ciddi
nefes darlığı ve kardiyopulmoner
arrest

Ölümünden yaklaşık 12 saat sonra
otopsi

Histolojik muayene eozinofilik

CASE REPORT

Penicillin-Induced Fulminant Myocarditis *A Case Report and Review of the Literature*

Mehdi Ben Khelil, MD,*† Youssef Chkirbene, MD,*† Mona Mlika, MD,†
Slim Haouet, MD,†‡ and Moncef Hamdoun, MD*†

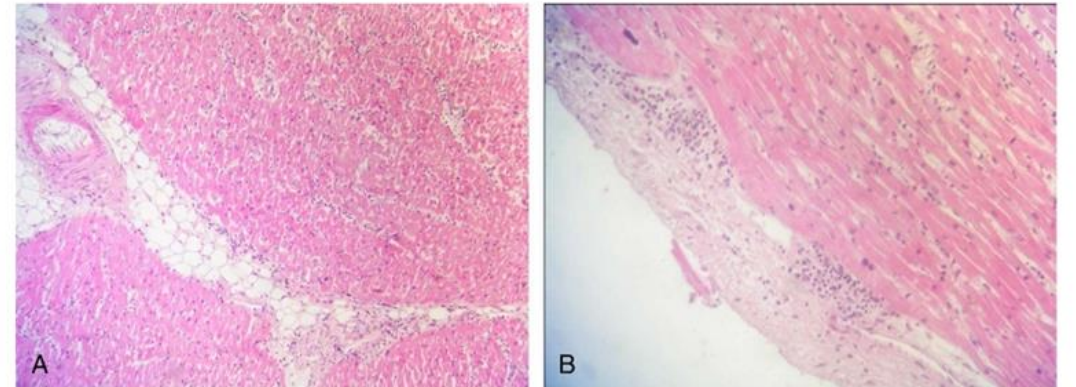


FIGURE 1. A, Widespread inflammatory infiltrate consisting predominantly of eosinophils (H&E, $\times 100$). B, Diffuse eosinophilic infiltrates in the interstitium and the endocardium (H&E, $\times 200$).

Table 1 Noncephalosporin drugs reported to have caused acute hypersensitivity myocarditis

Antibiotics	Diuretics
Amphotericin B	Acetazolamide
Ampicillin	Chlorthalidone
Chloramphenicol	Furosemide
Isoniazid	Hydrochlorothiazide
Para-aminosalicylic acid	Spironolactone
Penicillin	
Streptomycin	Vaccinations
Sulfadiazine	Anti-tetanus toxoid
Sulfisoxazole	Diphtheria, polio and tetanus vaccine
Tetracycline	Others
Antipsychotics	Amitrptylene
Clozapine	Aminophylline/theophylline
Anticonvulsants	Allopurinol
Carbamazepine	Colchicine
Phenindione	Digoxin
Phenobarbital	Diphenhydramine
Phenytoin	Ephedra
Antiinflammatory	Gefitinib
Diclofenac	Lidocaine
Indomethacin	Methyldopa
Oxyphenbutazone	Pranlukast
Phenylbutazone	Procainamide
Sulphasalazine	Quinidine
	Reserpine

Sefalosporin
dışında
akut
hipersentivite
miyokardit
yapan ilaçlar

DRESS Sendrom

33 yaş erkek

4 hafta önce sefaklor ve non
streoid antiinflamatuvar kullanımı

Renal yetmezlik, karaciğer
fonksiyon bozukluğu, ciddi
hipotansiyon, mekanik destek
gerektirecek LV disfonksiyonu

Miyokardit tanısı ile prednisolon
tedavi sonrası deri döküntüleri,
çoklu organ disfonksiyonu ve
kardiyak disfonksiyonda tam
düzelme

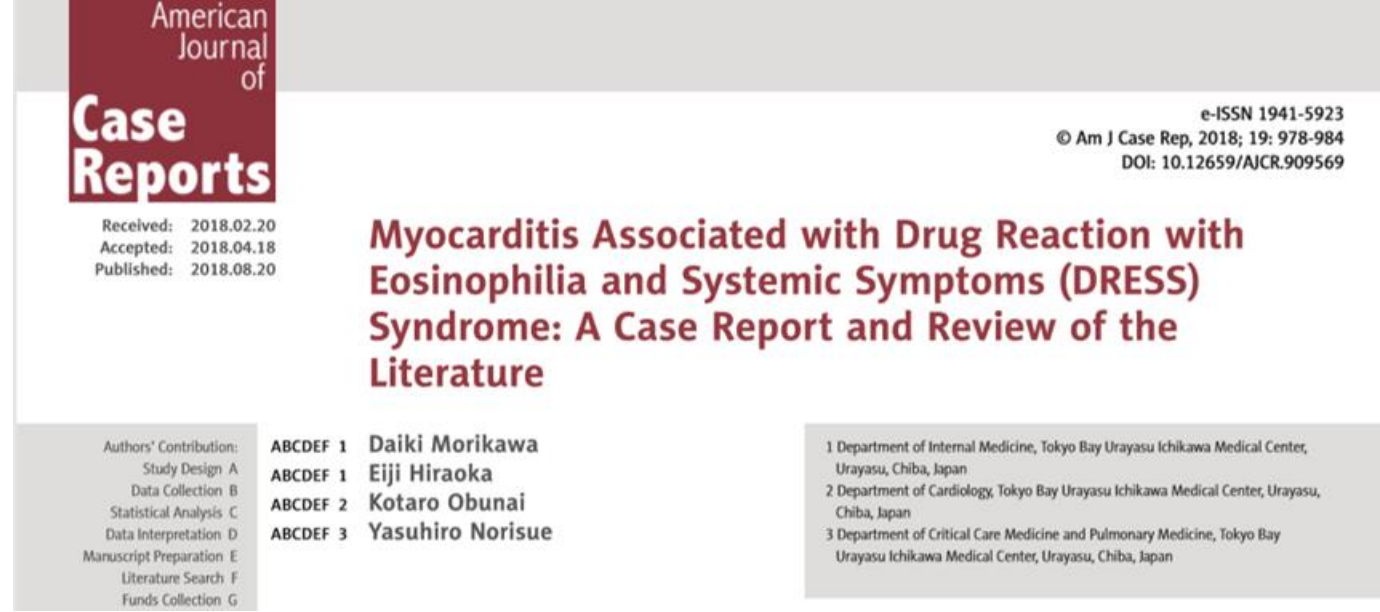


Table 2. Clinical characteristics of patients with drug reaction with eosinophilia and systemic symptoms (DRESS) on admission, and outcome, from the literature.

	All N=43		No corticosteroid use N=7		Corticosteroid use N=36		P-value*
Age mean (SD)	32	(±18)	30	(±26)	33	(±16)	0.80
Male, n (%)	20	(47%)	5	(71%)	15	(41%)	0.22
Hypotension** on admission, n (%)	24	(56%)	3	(42.9%)	21	(58.3%)	0.68
EF <30%, n (%)	14	(33%)	0	(0%)	14	(41%)	0.28
Other immunosuppression or IVIG treatment, n (%)	11	(26%)	0	(0%)	11	(31%)	0.31
Outcome							
In-hospital death, n (%)	19	(44%)	6	(85.7%)	13	(36%)	0.03
Full recovery of cardiac function, n (%)	21	(49%)	1	(14%)	20	(55%)	0.09

Table 3. Factors associated with in-hospital death for of patients with drug reaction with eosinophilia and systemic symptoms (DRESS), from the literature.

Factor	n	Death, n (%)	OR (unadjusted)*		OR (adjusted)**	
Age >50	6	1 (17%)	0.21	(0.02–1.9)		
Hypotension on admission***	24	9 (38%)	0.54	(0.16–1.8)		
EF <30%	15	5 (35%)	0.60	(0.16–2.2)	0.97	(0.24–3.9)
No corticosteroid	7	6 (86%)	10.6	(1.1–98) [#]	10.5	(1.1–104) [#]

DRESS Sendromu

Sefuroksim ilişkili Kounis Sendrom



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Journal of Infection and Public Health

journal homepage: <http://www.elsevier.com/locate/jiph>



Cefuroxime-associated Kounis syndrome with unique peculiarity in perioperative prophylaxis

Jie Gao, Yuan Gao, Jingjing Ma*



► Kounis Sendrom anafilaktik olayların akut koroner sendrom ile birlikteliği olarak tanımlanmaktadır.

37 yaş kadın

Preoperaif profilaksi için 1500 mg iv sefuroksim

Yaklaşık 75 dakika sonra anafilaktik şok

13 saat sonra ekg de st depresyonları görülmeye başlandı

- 2. gün eko LV ef%26
- 3.gün ventriküler taşikardi
- 4. gün koroner anjiyografi normal koroner arterler
- 11. gün LV ef normal

Kounis Sendrom

Previous reports of cefuroxime induced Kounis syndrome [4–7].

	Case 1 [4]	Case 2 [5]	Case 3 [6]	Case 4 [7]
Age (year)	70	40	61	90
Sex	Female	Male	Female	Male
Reason for admission	Gynaecological operation	NA	NA	Urinary tract infection
Administration route	Intravenous infusion	Oral	Oral	Intramuscular injection
History of allergy	No	No	NA	NA
Dose (mg)	750	500	250	750
Latent period (min)	1	5	10	10
Length of stay (day)	4	4	7	5
Past medical history	Increased cholesterol levels	No	Mild asthma	No
Symptoms	Retrosternal pain, erythematous rash, periorbital oedema, itching, vomiting, pale	Chest pain	Chest pain, nausea, vomiting, vertigo, erythema, dyspnea, anaphylactic shock	Thoracic pain, pruritic skin rash
Cardiac biomarker	Normal	Normal	cTnI 0.06 ng/mL, CK-MB 59 U/L	cTnI 4–22 ng/mL, CK-MB 42–85 U/L
ECG	ST-segment elevation in leads II, III, aVF with depression in leads I, aVL, V2	ST-segment elevation in leads D2, D3, aVF	ST-segment elevation in leads II, III, aVF with depression in leads I, aVL, V1–V3	ST-segment elevation in leads II, III, aVF, V4–V6
CAG	Normal	Plaques in the circumflex and right coronary artery	Plaques without significant stenosis	Plaques in the left anterior descending and circumflex artery
TTE	NA	Normal wall motion	Minimal inferior wall hypokinesia	Inferior wall hypokinesia



AORT ANEVİZMASI VE AORT DİSEKSİYONU

November 2015

Risk of Aortic Dissection and Aortic Aneurysm in Patients Taking Oral Fluoroquinolone

Chien-Chang Lee, MD, ScD^{1,2,3}; Meng-tse Gabriel Lee, PhD¹; Yueh-Sheng Chen, MD⁴; et al

» Author Affiliations | Article Information

JAMA Intern Med. 2015;175(11):1839-1847. doi:10.1001/jamainternmed.2015.5389

Table 1. Descriptive Characteristics of Patients With Aortic Aneurysm and/or Aortic Dissection and Controls

Characteristic ^a	Study Participants, No. (%) (n = 147 177) ^b		
	Aortic Aneurysm (n = 850)	Aortic Dissection (n = 662)	Controls (n = 147 700)
Demographics			
Male sex	630 (74.1)	473 (71.5)	107 600 (72.9)
Age, mean (SD), y	74.7 (11.7)	66.2 (14.5)	71.0 (13.7)
Index year			
2000	59 (6.9)	44 (6.7)	10 000 (6.8)
2001	60 (7.1)	46 (7.0)	10 500 (7.1)
2002	56 (6.6)	48 (7.3)	10 400 (7.0)
2003	76 (8.9)	53 (8.0)	12 300 (8.3)
2004	54 (6.4)	52 (7.9)	10 400 (7.0)
2005	62 (7.3)	63 (9.5)	12 500 (8.5)
2006	67 (7.9)	56 (8.5)	12 000 (8.1)
2007	78 (9.2)	60 (9.1)	13 200 (8.9)
2008	61 (7.2)	49 (7.4)	11 000 (7.5)
2009	76 (8.9)	58 (8.8)	12 900 (8.7)
2010	113 (13.3)	71 (10.7)	17 800 (12.1)
2011	88 (10.4)	62 (9.4)	14 700 (10.0)

Table 3. Rate Ratios Associated With Different Aortic Aneurysm and Aortic Dissection Definitions and Different Types of Fluoroquinolone Use

Type of Fluoroquinolone Use ^a	Effect Estimate, Rate Ratios (95% CI)	
	Matched on Age Group, Sex, and Year	Propensity Score Adjusted
Aortic aneurysm only		
Current	2.98 (2.05-4.32) ^b	2.36 (1.66-3.36) ^b
Past	1.45 (1.05-2.00) ^c	1.19 (0.87-1.62)
Any in prior year	1.88 (1.46-2.41) ^b	1.52 (1.19-1.94) ^b
Aortic dissection only		
Current	2.93 (1.79-4.80) ^b	2.55 (1.58-4.11) ^b
Past	2.27 (1.53-3.17) ^b	2.00 (1.44-2.79) ^b
Any in prior year	2.45 (1.85-3.25) ^b	2.15 (1.61-2.85) ^b
Aortic aneurysm undergoing surgery only		
Current	2.27 (0.92-5.58)	1.99 (0.79-4.98)
Past	1.11 (0.52-2.37)	1.02 (0.47-2.21)
Any in prior year	1.41 (0.78-2.54)	1.28 (0.69-2.35)
Aortic dissection undergoing surgery only		
Current	4.14 (1.25-13.67) ^c	3.50 (1.04-11.84) ^c
Past	0.48 (0.07-3.44)	0.42 (0.06-3.07)
Any in prior year	1.40 (0.51-3.89)	1.22 (0.43-3.46)
Aortic aneurysm or aortic dissection undergoing surgery		
Current	2.45 (1.15-5.27) ^c	2.15 (0.97-4.60)
Past	0.97 (0.49-1.99)	0.88 (0.43-1.82)
Any in prior year	1.35 (0.80-2.30)	1.21 (0.70-2.08)

Florokinolon
ve aort
anevrizması
aort
diseksiyonu

Florokinolon Aort anevrizması Aort diseksiyonu

Son 60 gün içinde
florokinolon kullanımı aort
anevrizma ve aort
diseksiyon riskini 2 kat
arttırır.

Table 4. Risk of Aortic Aneurysm or Aortic Dissection Associated With Increasing Duration of Fluoroquinolone Use

Duration of Fluoroquinolone Use, d	Case/Person-years, No. (Incidence Rate, %)	Propensity Score-Adjusted Rate Ratio (95% CI)
<3 [Reference]	1432/147 495 (0.97)	1 [Reference]
3-14	33/1271 (2.60)	1.60 (1.10-2.52) ^a
>14	12/411 (2.92)	1.81 (0.91-3.17)

^a $P < .05$.

Siprofloksasin ve akut aort kapak hasarı

Önerilen kolajen hasar mekanizmaları arasında, matris metaloproteinazlar gibi bozundurucu enzimlerin yukarı regülasyonu ve özel kolajen üreten fibroblastların inhibisyonu bulunmaktadır. Tip I ve tip II kollajen, Aşil tendonu, aort ve aort kapaklarındaki kollajenin çoğunluğunu içerir.

76 yaş erkek

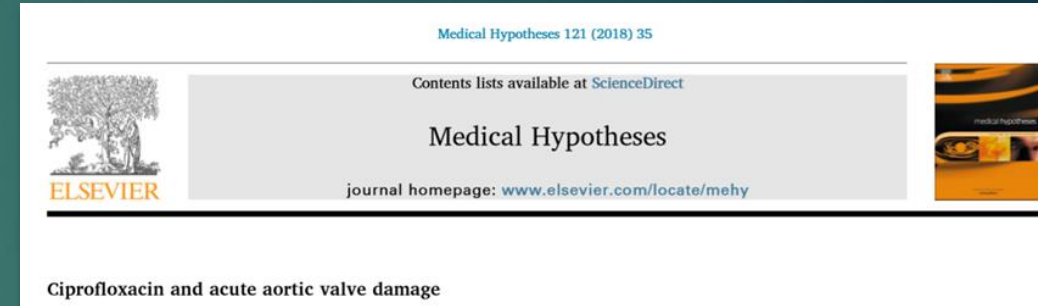
lokal enfekte diz ekleminin değiştirilmesi Kloksasilin ve Rifampisin başlanıyor

10 gün sonra kloksasilin siprofloksasin ile değiştiriliyor.

2 gün sonra ani gelişen kardiyak dekompanseasyon

Endokardit, sepsis, mitral darlık vb izlenmiyor. Biküspit aort kapağın prolabe olduğu izleniyor. Tekrarlanan kan kültürleri negatif

Florokinolon kullanımına bağlı biküspit aort kapakta akut dejeneratif değişiklikler olduğu düşünülüyor.



Florokinolon FDA UYARISI



U.S. Food and Drug Administration
Protecting and Promoting Your Health

Drug Safety Communications

This information is an update to the FDA announcement issued on [May 10, 2017](#)

FDA warns about increased risk of ruptures or tears in the aorta blood vessel with fluoroquinolone antibiotics in certain patients

Safety Announcement

[12-20-2018] A U.S. Food and Drug Administration (FDA) review found that fluoroquinolone antibiotics can increase the occurrence of rare but serious events of ruptures or tears in the main artery of the body, called the aorta. These tears, called aortic dissections, or ruptures of an aortic aneurysm can lead to dangerous bleeding or even death. They can occur with fluoroquinolones for systemic use given by mouth or through an injection.

Fluoroquinolones should not be used in patients at increased risk unless there are no other treatment options available. People at increased risk include those with a history of blockages or aneurysms (abnormal bulges) of the aorta or other blood vessels, high blood pressure, certain genetic disorders that involve blood vessel changes, and the elderly. We are requiring that a new warning about this risk be added to the [prescribing information](#) and patient [Medication Guide](#) for all fluoroquinolones.

Nadir ama ciddi

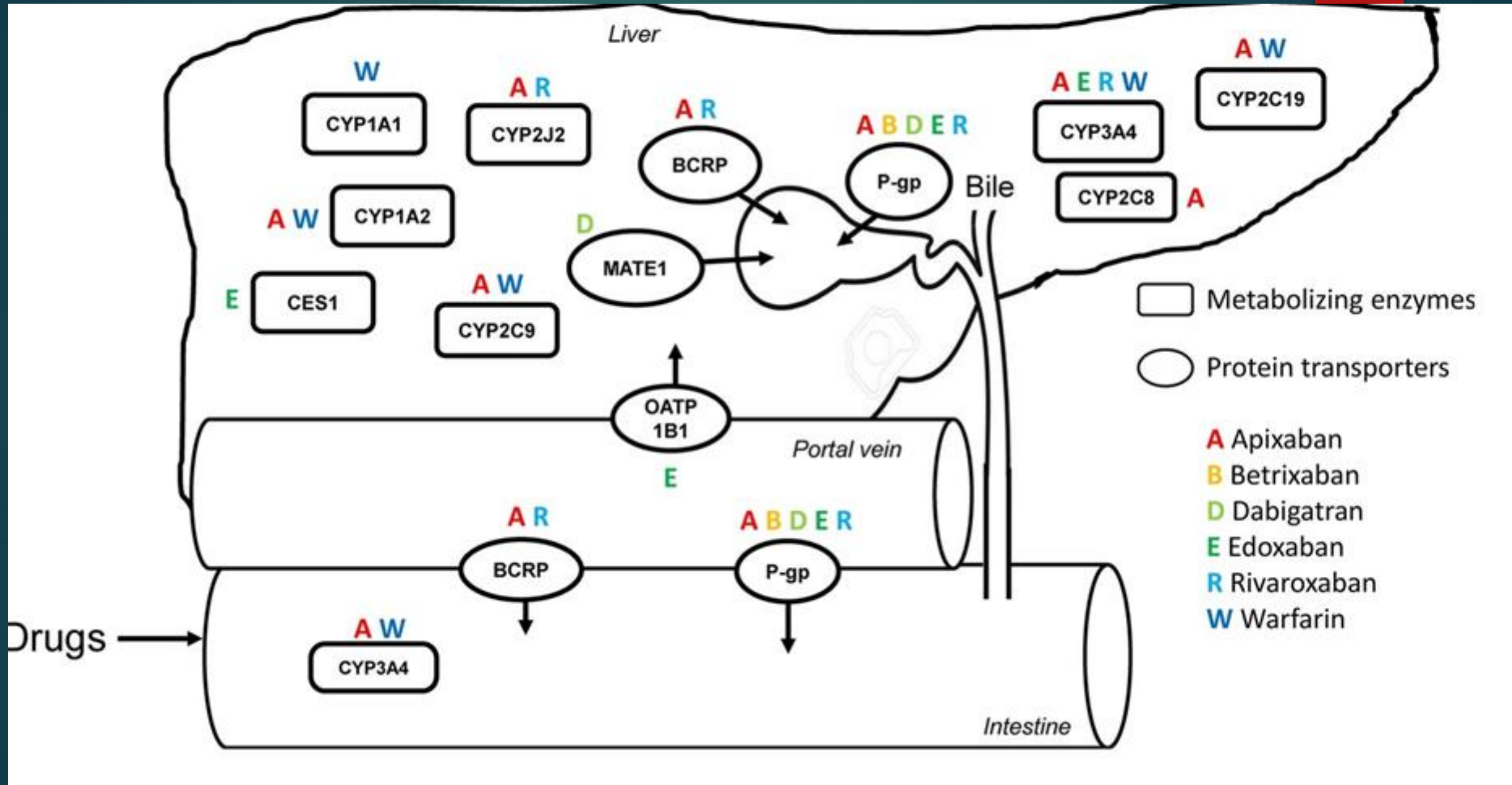
Aort diseksiyon ve aort anevrizma
r  pt  r

Tehlikeli kanama ve   l  m

Oral ya da enjeksiyon

Florokinolonlar di  er tedavi
v  ntemlerinin m  mk  n olmad  ı
durumlar dışında artmış riski bulunan
hastalarda kullanılmamalıdır (Yaşlı,
aort anevrizması bulunan,
hipertansif, damarlarda de  isikliklere
sebebi olan aenetik rahatsızlı  ı
bulunan hastalar).

Antikoagülanlar



Varfarinin farmakokinetik ilaç reaksiyonları

Cytochrome P450	Inhibitors	Inducers
CYP2C9	amiodarone , capecitabine, cotrimoxazole, etravirine, fluconazole , fluvastatin, fluvoxamine , isoniazid , metronidazole, miconazole , oxandrolone, sulfinpyrazone, tigecycline, voriconazole , zafirlukast	aprepitant, bosentan, carbamazepine, phenobarbital, rifampicin
CYP1A2	acyclovir, allopurinol, amiodarone , caffeine, cimetidine, ciprofloxacin , disulfiram, enoxacin, famotidine, fluvoxamine , methoxsalen, mexiletine, miconazole , norfloxacin, oral contraceptives, phenylpropanolamine, propafenone , propranolol , terbinafine, thiabendazole, ticlopidine , verapamil, voriconazole , zileuton	montelukast, moricizine, omeprazole, phenobarbital, phenytoin
CYP3A4	alprazolam, amiodarone , amlodipine, amprenavir, aprepitant, atorvastatin, atazanavir, bicalutamide, cilostazol , cimetidine, ciprofloxacin, clarithromycin, clofibrate , conivaptan, cyclosporine, darunavir/ritonavir, diltiazem , dronedarone , erythromycin, fenofibrate , fluconazole , fluoxetine , fluvoxamine , fosamprenavir, imatinib, indinavir, isoniazid , itraconazole, ketoconazole, lopinavir/ritonavir, nefazodone, nelfinavir, nilotinib, oral contraceptives, posaconazole, propafenone , ranitidine, ranolazine, ritonavir, saquinavir, telithromycin, tipranavir, voriconazole , zileuton	armodafinil, amprenavir, aprepitant, bosentan, carbamazepine, efavirenz, etravirine, modafinil, nafcillin, phenytoin, pioglitazone, prednisone, rifampicin, rifampicin , rufinamide

Varfarin dışı oral antikoagülanlar

	apixaban	betrixaban *	dabigatran etexilate	edoxaban	rivaroxaban
Antibiotics					
azithromycin	10	↑	8	5	9
clarithromycin	↑ ¹		↑ ⁶	5	↑ ³
erythromycin	↑ ²		8	↑ ⁵	↑ ⁹
rifampicin	↓ ¹		↓ ¹	↓ ³	↓ ¹
Antimycotics					
fluconazole	10		10	10	↑ ¹⁰
ketoconazole	↑ ¹	↑	↑ ⁷	↑ ⁵	↑ ¹
itraconazole	1		8	5	↑ ¹
posaconazole	10		10	10	↑ ¹
voriconazole	10		10	10	↑ ¹
Antiviral Drugs					
cobicistat	10		↑ ¹⁰	10	10
ritonavir	1		8	5	↑ ¹
telaprevir	2		8	5	10

• Gri: İlgili DDI veya doz ayarlaması gerekmez.

• Sarı: Dikkat edilmesi önerilir.

• Turuncu: Doz ve posoloji ayarını veya yakın klinik izlemeyi düşünün.

• Kırmızı: Kontrendikedir / önerilmez.

En çok bildiğimiz
En çok güvendiğimiz
En çok kullandığımız
En eski
En yeni
En ucuz
En pahalı

.....

İyi niyetle reçete ettiğimiz **TEK** bir ilaç bile
hastamızı kaybetmemize neden olabilir.



TEŞEKKÜRLER

