



23. ULUSAL KONGRESİ

Göğüs Kalp Damar Anestezi ve Yoğun Bakım Derneği

25-28 Mayıs 2017
Marriot Hotel Asia
İSTANBUL

Antiplatelet Kullanan Hasta

Mehmet TUĞRUL



İstanbul Üniversitesi
İSTANBUL TIP FAKÜLTESİ



188. yıl

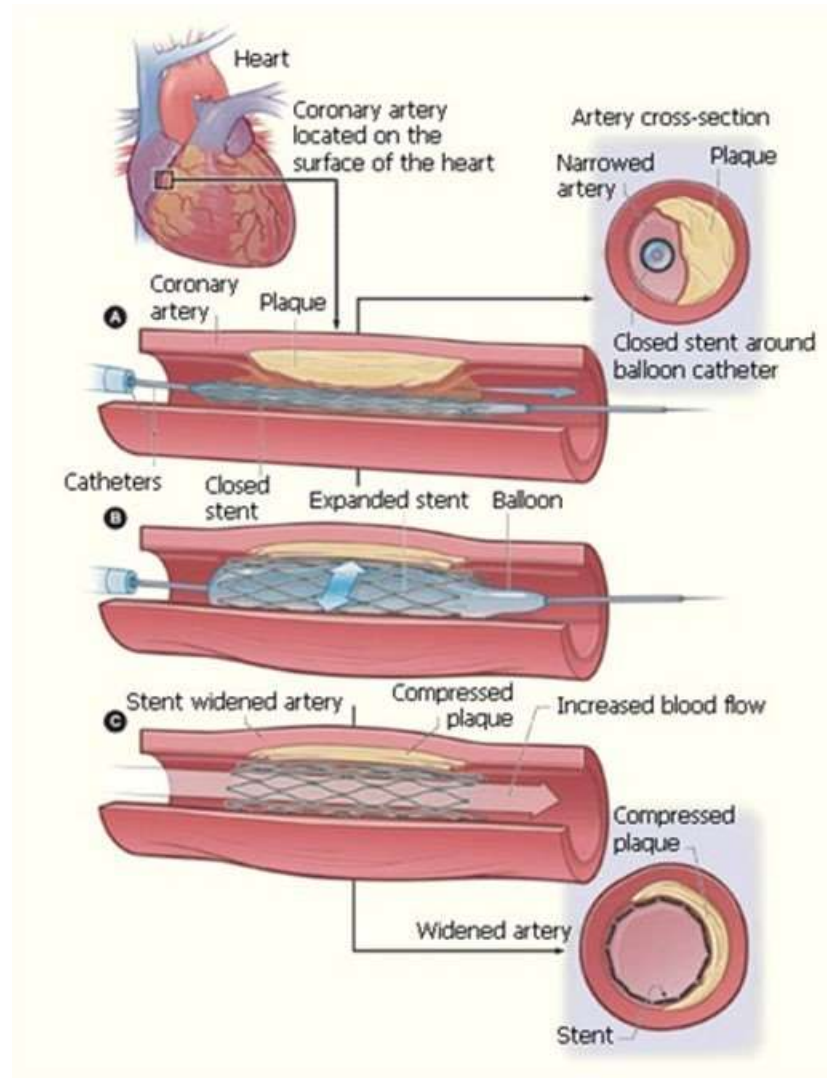
Endikasyonlar

- Akut Koroner Sendrom
- İKH, SAP
- Angioplasti
- CABG sonrası
- TIA, SVA
- Karotis operasyonları
- Periferik damar hastalıkları
- Stentler

- Perkütan koroner girişim yapılan hastaların %5' i 1 yıl içinde non-kardiyak cerrahi geçirmektedir
- Bildirilen stent trombozu olgularının yaklaşık %40' ı perioperatif süreçte gerçekleşmektedir
- Stent trombozuna bağlı MI yüksek mortalite ile seyretmektedir

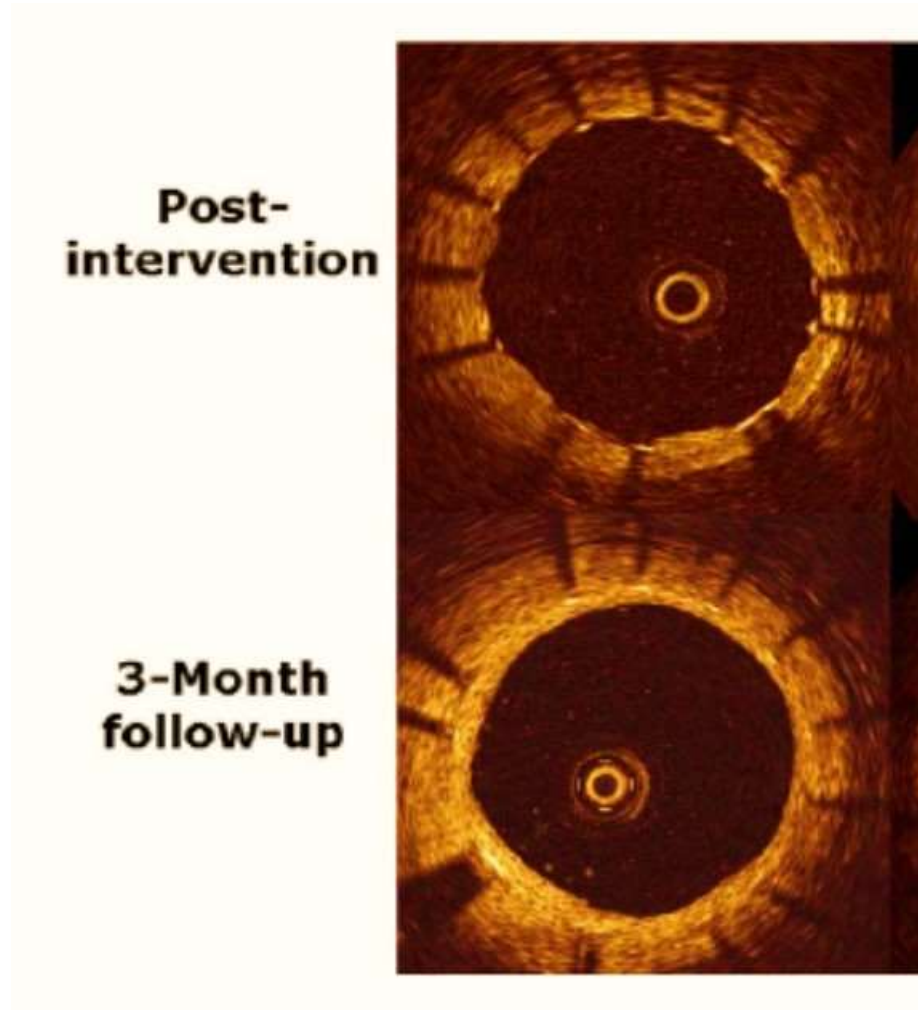


CORONARY STENTS

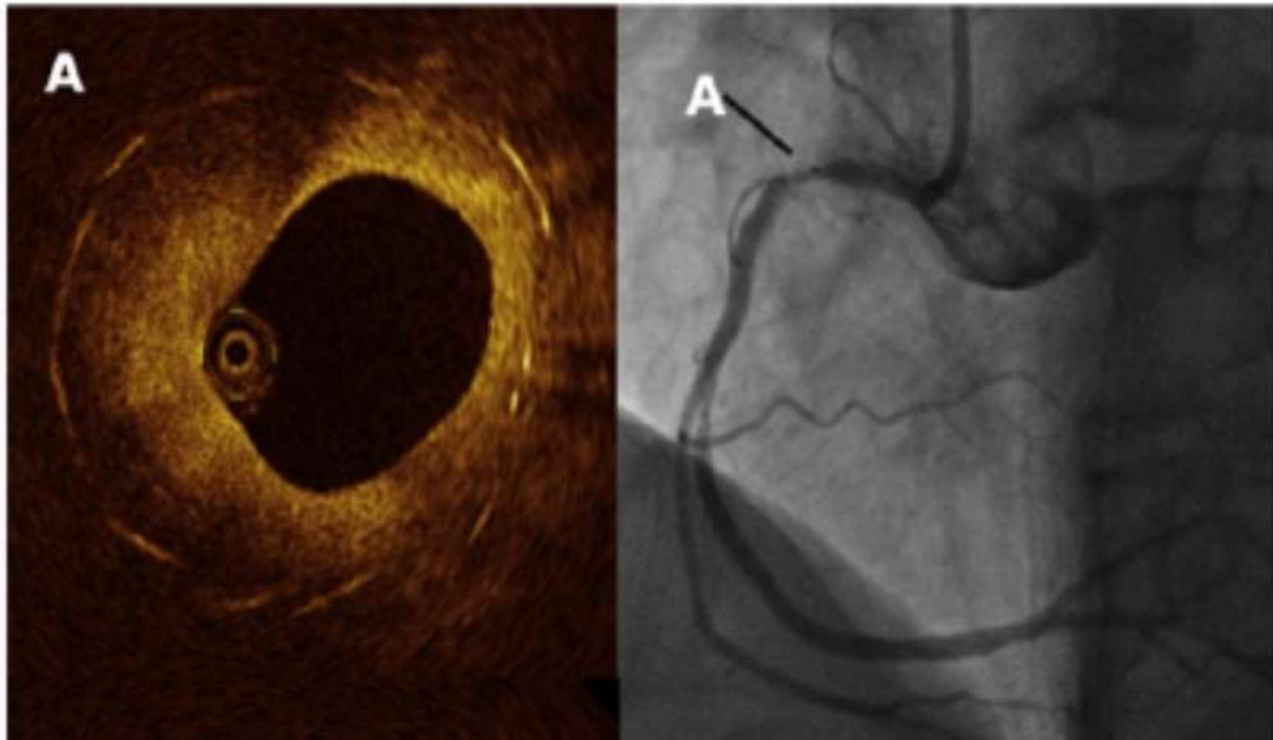


- Bare Metal stents (BMS)
- Drug eluting stents (DES)

Re-endotelizasyon

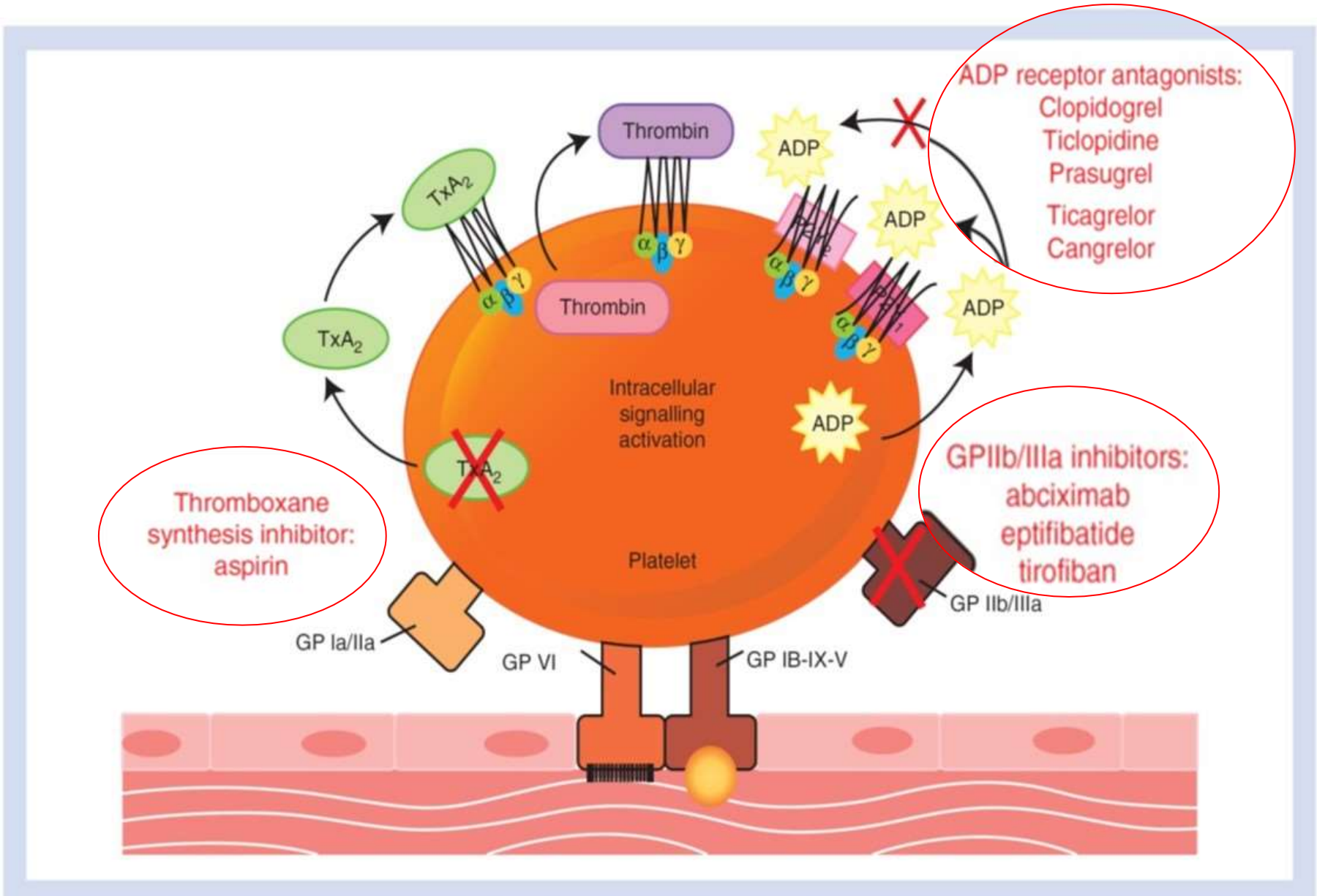


Restenoz (neo-intimal hiperplazi)



Değişen Gündem

- BMS → Restenoz
- DES → DAPT ve stent trombozu
- Hedef → Fonksiyonel endotelial yüzey



Thromboxane synthesis inhibitor: aspirin

ADP receptor antagonists:
Clopidogrel
Ticlopidine
Prasugrel
Ticagrelor
Cangrelor

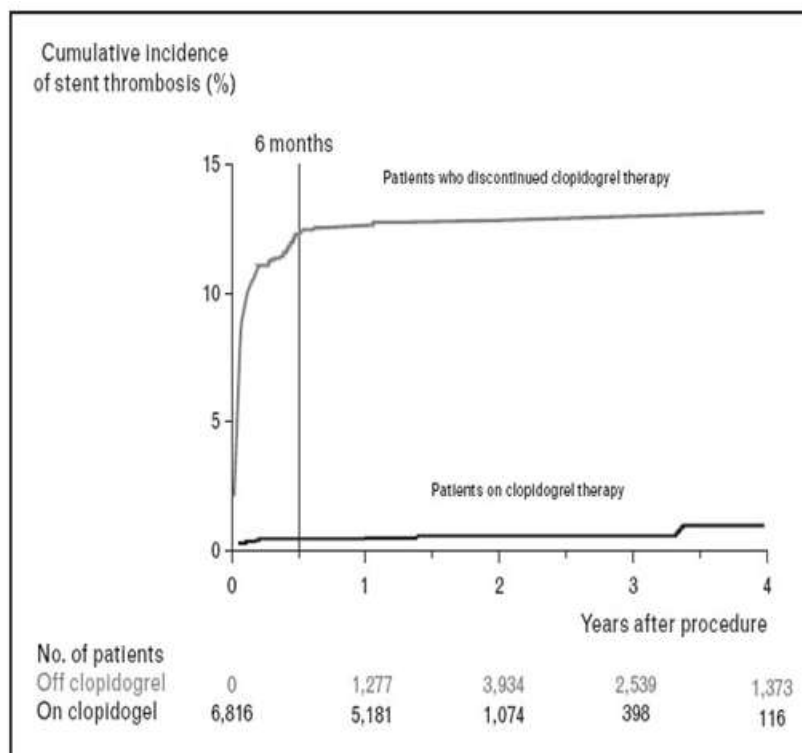
GPIIb/IIIa inhibitors:
abciximab
eptifibatide
tirofiban

Stent trombozu risk faktörleri

- Antiplatelet tedavinin kesilmesi
- Perioperatif dönem
- Antiplatelet tedavinin perioperatif dönemde kesilmesi
- Yetersiz re-endotelizasyon süresi ve ameliyat zamanlaması
- Hastaya ait riskler
- Perkütan girişime ait riskler

Stent thrombosis after drug-eluting stent implantation: incidence, timing, and relation to discontinuation of clopidogrel therapy over a 4-year period

Stefanie Schulz^{1*}, Tibor Schuster², Julinda Mehilli¹, Robert A. Byrne¹, Julia Ellert¹, Steffen Massberg¹, Julia Goedel¹, Olga Bruskina¹, Kurt Ulm², Albert Schömig^{1,3}, and Adnan Kastrati¹



Perioperatif süreçte koagülasyona eğilim

- Trombosit aktivasyonu, adhezyon artışı
- Fibrinoliz azalması (PAI-1 artışı)
- Prokoagülan faktörlerde artış (FVII, X, trombin)
- Sitokin ve inflamatuvar medyatörlerde artış
- Sempatik aktivite artışı ve vazospazm

Perioperative management of oral antiplatelet therapy and clinical outcomes in coronary stent patients undergoing surgery

Results of a multicentre registry

Roberta Rossini¹; Giuseppe Musumeci¹; Davide Capodanno²; Corrado Lettieri³; Ugo Limbruno⁴; Giuseppe Tarantini⁵; Nicolina Russo¹; Paolo Calabria⁴; Michele Romano³; Ana Inashvili¹; Vasile Sirbu¹; Giulio Guagliumi¹; Orazio Valsecchi¹; Michele Senni¹; Antonello Gavazzi¹; Dominick J. Angiolillo⁶

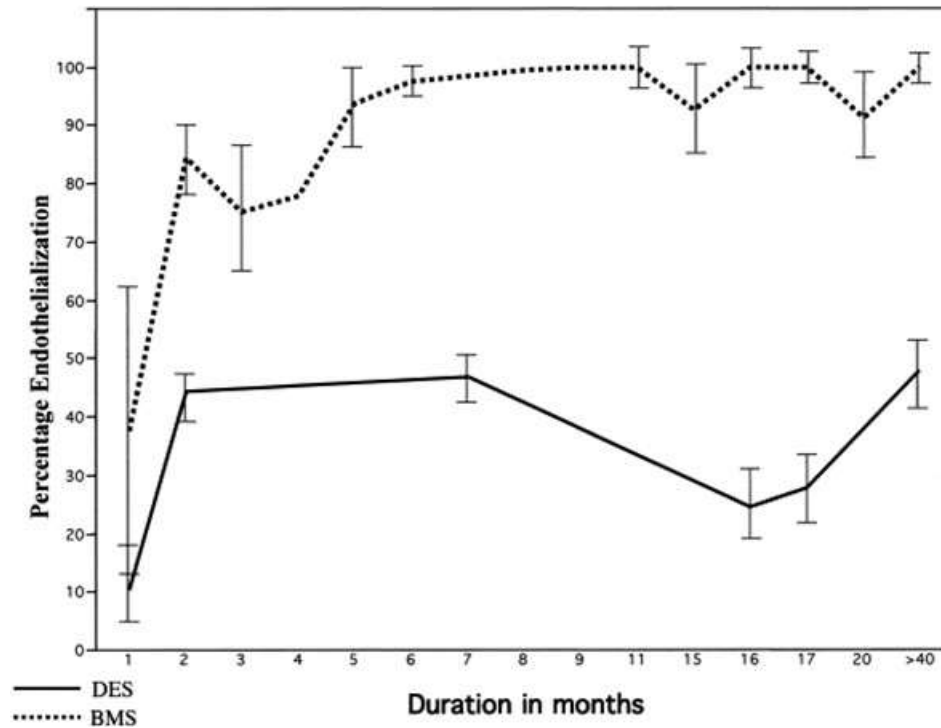
Thromb Haemost 2015

- 2003-2011 retrospektif
- Perioperatif süreçte DAPT veya ASA vs antiplatelet kesilmesi
- 30-günlük MACE

| Variable | Overall (N=666) | Antiplatelet discontinuation (N=371) | No Antiplatelet discontinuation (N=295) | P value |
|---------------------------------------|-----------------|--------------------------------------|---|---------|
| Ischaemic Endpoints | | | | |
| MACE, n (%) | 31 (4.2) | 30 (7.5) | 1 (0.3) | <0.001 |
| Cardiac death, n (%) | 11 (1.7) | 10 (2.7) | 1 (0.3) | 0.027 |
| Myocardial Infarction, n (%) | 15 (2.3) | 15 (4.0) | 0 (0) | <0.001 |
| ACS leading to hospitalisation, n (%) | 13 (2.0) | 10 (2.7) | 3 (1.0) | 0.120 |
| Stroke, n (%) | 2 (0.3) | 2 (0.5) | 0 (0) | 0.51 |
| Stent thrombosis, n (%) | 8 (1.2) | 7 (1.9) | 1 (0.3) | 0.08 |
| Bleeding Endpoints | | | | |
| BARC bleeding ≥2, n (%) | 135 (20.4) | 95 (25.6) | 41 (13.9) | <0.001 |
| BARC bleeding 1, n (%) | 11 (1.7) | 5 (1.3) | 6 (2.0) | 0.55 |
| BARC bleeding 2, n (%) | 1 (0.1) | 0 (0) | 1 (0.3) | 0.44 |
| BARC bleeding 3, n (%) | 99 (14.9) | 65 (17.5) | 34 (11.5) | 0.031 |
| BARC bleeding 4, n (%) | 31 (4.7) | 27 (7.3) | 4 (1.4) | <0.001 |
| BARC bleeding 5, n (%) | 5 (0.8) | 3 (0.8) | 2 (0.7) | 1.00 |

ACS, acute coronary syndrome; BARC, Bleeding Academic Research Consortium; MACCE, major adverse cardiac or cerebrovascular events.

Yetersiz re-endootelizasyon süresi ve ameliyat zamanlaması

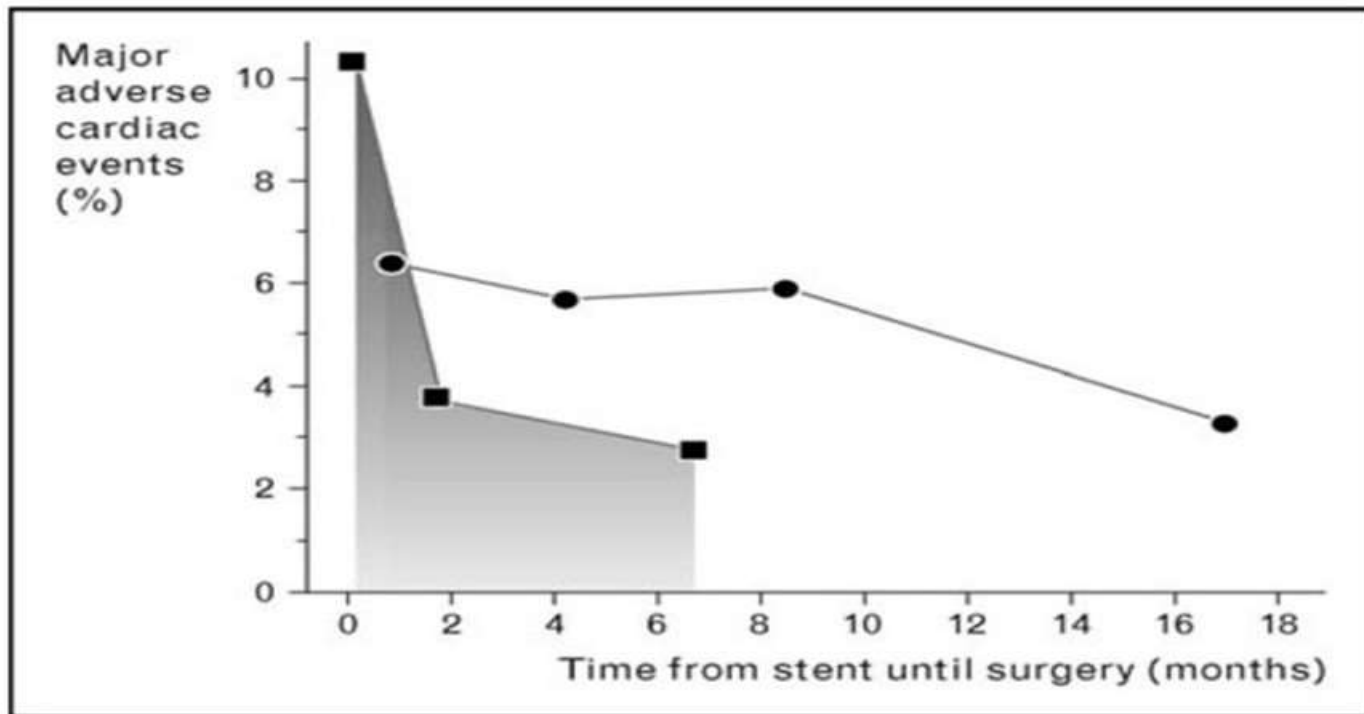


Michael Joner, Alope V. Finn, Andrew Farb, Erik K. Mont, Frank D. Kolodgie, Elena Ladich, Robert Kutys, Kristi Skorija, Herman K. Gold, Renu Virmani

Pathology of Drug-Eluting Stents in Humans : Delayed Healing and Late Thrombotic Risk

Journal of the American College of Cardiology, Volume 48, Issue 1, 2006, 193–202

Rate of major adverse cardiac events in relation to time elapsed from stent insertion to noncardiac surgery



Stent trombozu risk faktörleri

| | Factors | Hazard Ratio | |
|----------------------------------|----------------------------------|--------------|-----------|
| Patient | Acute MI | 1.80–3.91 | |
| | Age (per y) | 1.02–1.05 | |
| | Diabetes mellitus | 2.10–4.74 | |
| | LVEF <40% | 1.09–3.51 | |
| | Prior MI | 1.40–2.50 | |
| | Prior PCI | 2.36 | |
| | Renal insufficiency | 3.98–6.49 | |
| | Smoking | 1.66–2.63 | |
| | Discontinuation of clopidogrel | 3.20–89.78 | |
| | Procedure | LAD stenting | 2.73 |
| Left main stenting | | 1.55 | |
| Multiple stenting | | 2.35–2.50 | |
| Multiple vessels treated | | 2.05 | |
| Residual thrombus | | 6.50 | |
| Stent diameter (per mm decrease) | | 2.71 | |
| Stent overlap | | 2.38 | |
| Small vessel diameter post-PCI | | 1.72–4.50 | |
| Lesion | | Aneurysm | 2.54 |
| | | Bifurcation | 2.39–6.42 |
| | Bypass graft stenosis | 4.30 | |
| | In-stent restenosis | 4.75 | |
| | Lesion length (>28 mm) | 2.34–2.42 | |
| | Moderate or severe calcification | 1.60 | |
| | Multiple vessel disease | 1.60 | |
| | TIMI flow 0 or 1 | 1.59 | |
| Plaque ulceration | 2.25 | | |

All hazard ratios were significant with $P < 0.05$.

LAD indicates left anterior descending; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIMI, Thrombolysis In Myocardial Infarction.

Adapted with permission from *Curr Treat Options Cardiovasc Med* 2012;14: 91–107.

Algoritma ve kılavuzlar

- Hastada **stent trombozu** riski ile ameliyatın **kanama riskini** değerlendirir ve **mümkünse** perioperatif dönemde aktüel antiplatelet tedaviyi sürdür

Tromboz riski ve Kanama riski

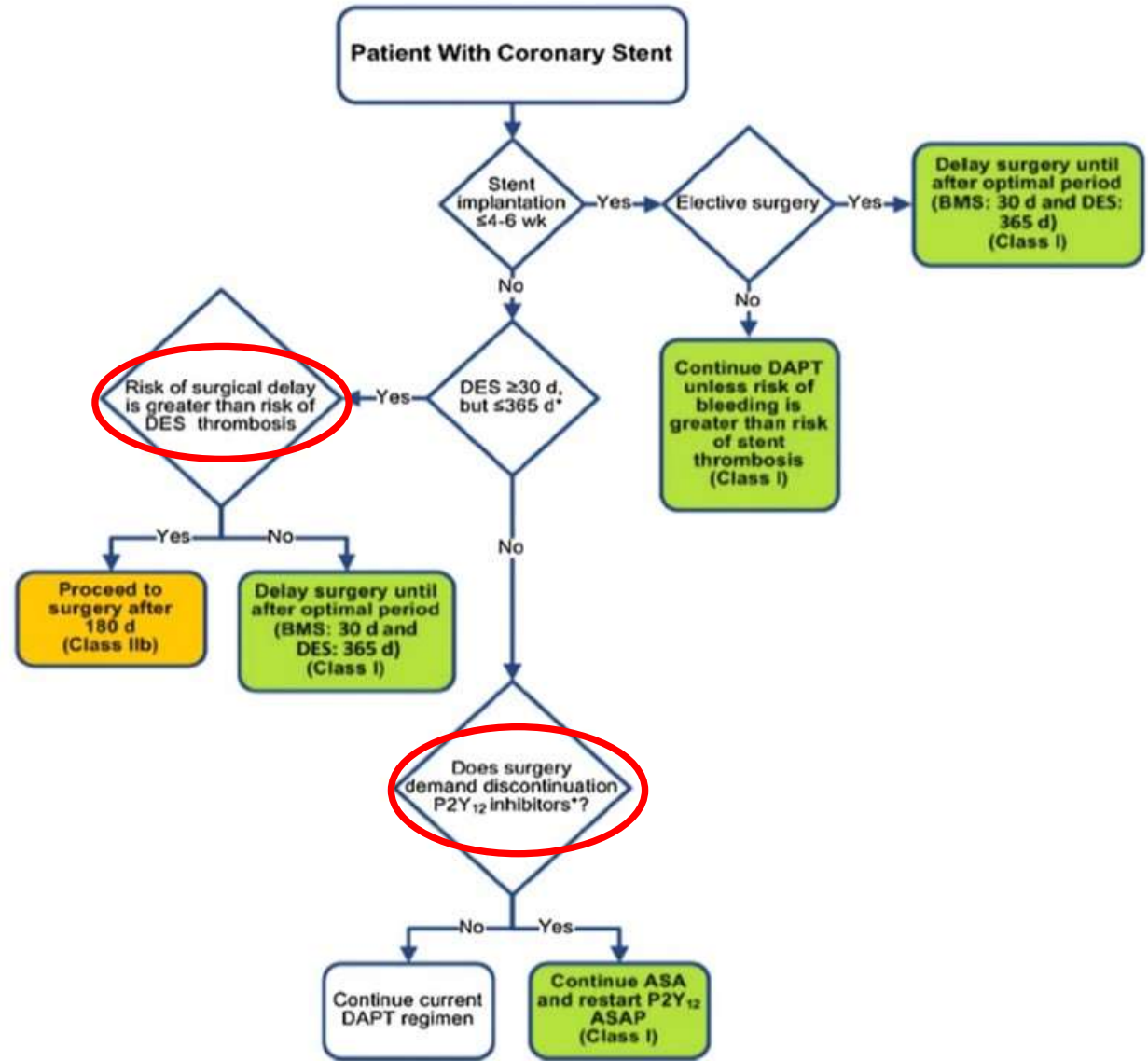
| | Minor | Moderate | Major |
|-------------------|--|--|---|
| Haemorrhagic risk | Transfusion usually not needed. Minor plastic/general/ortho surgery; biopsies, tooth extraction, surgery of the anterior segment of the eye | Transfusion usually needed. Cardiac, major ortho/visceral/ENT/urology or reconstructive surgery | Possible bleeding in an enclosed space. Neurosurgery, spinal surgery, surgery of the posterior segment of eye |
| Thrombotic risk | >6 months after AMI, CABG, percutaneous coronariography, BMS, coronary surgery, CVS (>12 months if complications) | 6–24 weeks after AMI, CABG, BMS, CVS (6–12 months if complications or high risk or diabetic or low LVEF) >12 months after DES | <6 weeks after AMI, CABG, BMS, CVS (<6 months if complications) <12 months after DES |

AMI, acute myocardial infarction; BMS, bare metal stent; CABG, coronary artery bypass grafting; CVS, cerebrovascular stroke; DES, drug-eluting stent; ENT, ear–nose–throat surgery; LVEF, left ventricular ejection fraction; ortho, orthopaedic surgery.

Hasta bazlı karar

- Ameliyatın kanama riski
- Cerrah
- Anestezist
- Konsültan kardiyolog
- Primer kardiyolog
- Eldeki veriler
- Hastaya ait riskler
- Perkütan girişime ait riskler
- Ameliyat zamanlaması

2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery



Kılavuzlar

- Elektif ameliyatları ertele (Vulnerable period)
 - BMS 1 ay, DES 6 ay
 - MI sonrası BMS ve DES için 1 yıl
- Acil ve yarı-elektif işlemler aktüel antiplatelet tedavi altında
- Riskli dönem sonrası
 - Antiplatelet tedaviyi sürdürmeye çalış
 - Mümkün değilse aspirine devam et
 - Mümkün değilse ikisini de kes
 - Her iki risk de yüksek ise «köprüleme»

«Köprüleme»

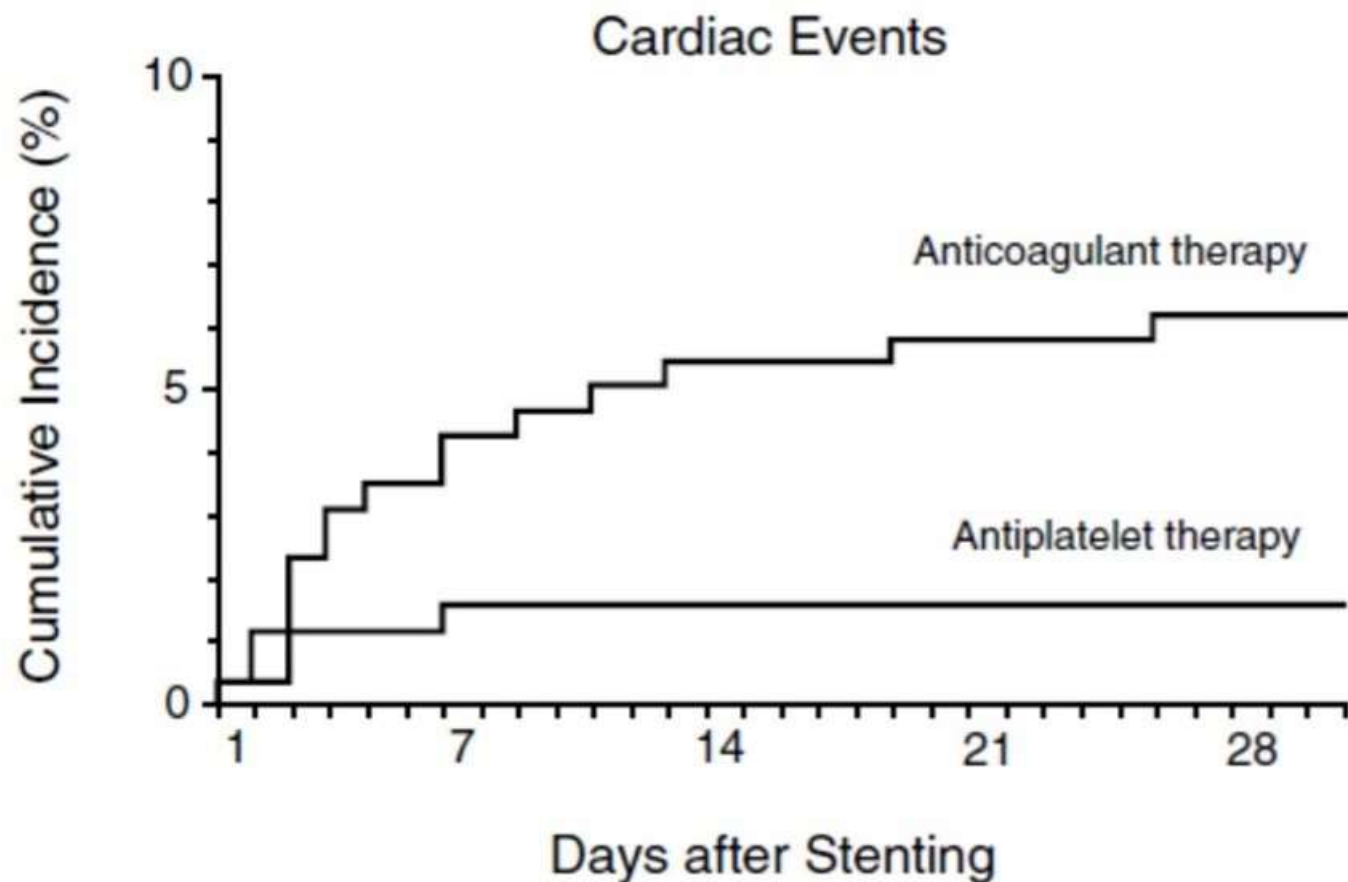
- Heparin, LMWH ???
- Tirofiban
- Cangrelor

Arteriyel Tromboz

- Trombosit bazlı olay
- Fraksiyone olmayan heparin trombositleri uyarır ve zararlı olabilir
- LMWH trombositlere etkisi yok

A RANDOMIZED COMPARISON OF ANTIPLATELET AND ANTICOAGULANT THERAPY AFTER THE PLACEMENT OF CORONARY-ARTERY STENTS

ALBERT SCHÖMIG, M.D., FRANZ-JOSEF NEUMANN, M.D., ADNAN KASTRATI, M.D., HELMUT SCHÜHLEN, M.D.,
RUDOLF BLASINI, M.D., MARTIN HADAMITZKY, M.D., HANNA WALTER, M.D.,
EVA-MARIA ZITZMANN-ROTH, M.D., GERT RICHARDT, M.D., ECKHARD ALT, M.D.,
CLAUS SCHMITT, M.D., AND KURT ULM, PH.D.



Impact of bridging with perioperative low-molecular-weight heparin on cardiac and bleeding outcomes of stented patients undergoing non-cardiac surgery

Davide Capodanno¹; Giuseppe Musumeci²; Corrado Lettieri³; Ugo Limbruno⁴; Michele Senni²; Giulio Guagliumi²; Orazio Valsecchi²; Dominick J. Angiolillo⁵; Roberta Rossini²

¹Division of Cardiology, Ferrarotto Hospital, University of Catania, Catania, Italy; ²Cardiovascular Department, Azienda Ospedaliera Papa Giovanni XXIII, Bergamo, Italy; ³Carlo Poma Hospital, Mantova, Italy; ⁴Misericordia Hospital, Department of Cardiology, Grosseto, Italy; ⁵University of Florida College of Medicine, University of Florida, Jacksonville, Florida, USA

Thromb Haemost 2015

- 2003-2012 retrospektif
- DAPT veya ASA vs LMWH köprüleme
- 30-günlük kardiyak ölüm, ACS, MI, strok

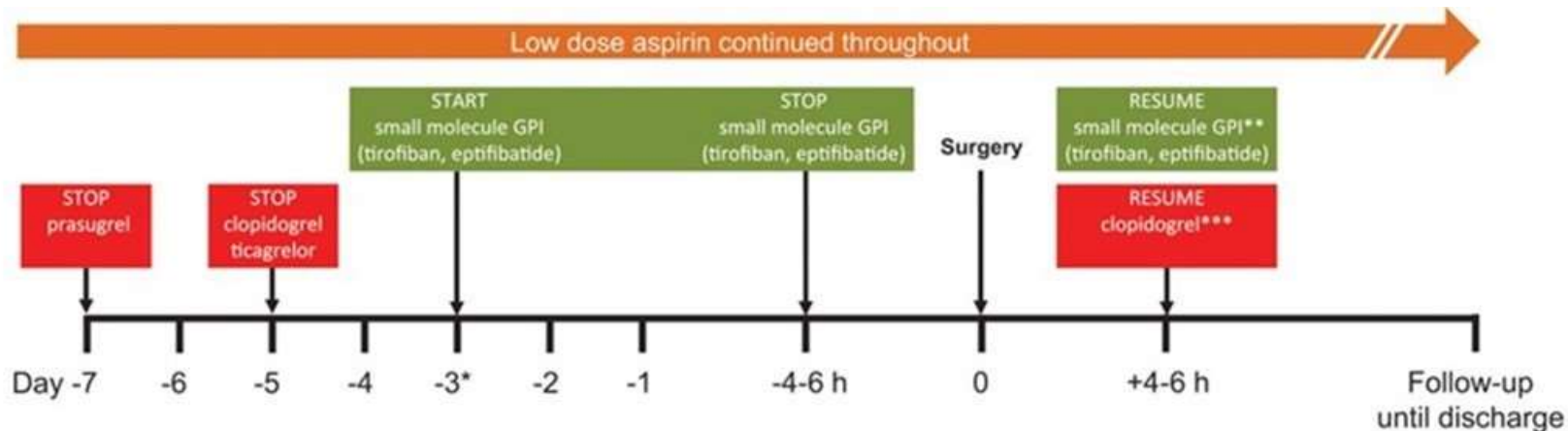
| Variable | Overall Series | | | | Propensity-matched Pairs | | |
|---------------------------|--------------------|-----------------|--------------------|---------|--------------------------|--------------------|---------|
| | Overall (N=515) | LMWH (N=251) | No LMWH (N=264) | P value | LMWH (N=179) | No LMWH (N=179) | P value |
| PCI details | | | | | | | |
| UA/NSTEMI, n (%) | 166 (32.2) | 76 (30.3) | 90 (24.1) | 0.36 | 56 (31.3) | 62 (34.6) | 0.50 |
| STEMI, n (%) | 87 (16.9) | 48 (19.1) | 39 (14.8) | 0.19 | 25 (14.0) | 26 (14.5) | 0.88 |
| Femoral access, n (%) | 268 (52.0) | 138 (55.0) | 150 (49.2) | 0.19 | 94 (52.5) | 97 (54.2) | 0.75 |
| DES, n (%) | 314 (61.0) | 134 (53.4) | 180 (68.2) | 0.001 | 100 (55.9) | 115 (64.2) | 0.11 |
| Bifurcation lesion, n (%) | 19 (3.7) | 10 (4.0) | 9 (3.4) | 0.73 | 8 (4.5) | 9 (5.0) | 0.80 |
| Number of stents, n±SD | 1.7±0.9 | 1.6±0.9 | 1.9±0.9 | 0.002 | 1.7±1.0 | 1.7±0.9 | 0.60 |
| Stent length, mm±SD | 32.9±21.2 | 30.7±20.8 | 35.0±21.5 | 0.02 | 31.6±22.1 | 31.6±18.7 | 0.98 |

| Variable | Overall Series | | | | Propensity-matched Pairs | | |
|---------------------------------------|--------------------|-----------------|--------------------|---------|--------------------------|--------------------|---------|
| | Overall (N=515) | LMWH (N=251) | No LMWH (N=264) | P value | LMWH (N=179) | No LMWH (N=179) | P value |
| Ischaemic Endpoints | | | | | | | |
| MACCE, n (%) | 21 (4.1) | 18 (7.2) | 3 (1.1) | 0.001 | 14 (7.8) | 1 (0.6) | 0.001 |
| Cardiac death, n (%) | 3 (0.6) | 3 (1.2) | 0 (0) | 0.12 | 3 (1.7) | 0 (0) | 0.25 |
| Myocardial Infarction, n (%) | 12 (2.3) | 12 (4.8) | 0 (0) | <0.001 | 9 (5.0) | 0 (0) | 0.004 |
| ACS leading to hospitalization, n (%) | 4 (0.8) | 2 (0.8) | 2 (0.8) | 1.00 | 2 (1.1) | 1 (0.6) | 1.00 |
| Stroke, n (%) | 2 (0.4) | 2 (0.8) | 0 (0) | 0.24 | 2 (1.1) | 0 (0) | 0.50 |
| Stent thrombosis, n (%) | 4 (0.8) | 4 (1.6) | 0 (0) | 0.06 | 2 (1.1) | 0 (0) | 0.50 |
| Bleeding Endpoints | | | | | | | |
| BARC bleeding ≥ 2 , n (%) | 86 (16.7) | 55 (21.9) | 31 (11.7) | 0.002 | 40 (22.3) | 24 (13.4) | 0.027 |
| BARC bleeding 1, n (%) | 9 (1.7) | 4 (1.6) | 5 (1.9) | 1.00 | 4 (2.2) | 2 (1.1) | 0.69 |
| BARC bleeding 2, n (%) | 1 (0.2) | 0 (0) | 1 (0.4) | 1.00 | 0 (0) | 1 (.6) | 1.00 |
| BARC bleeding 3, n (%) | 84 (16.3) | 54 (21.5) | 30 (11.4) | 0.002 | 39 (21.8) | 23 (12.8) | 0.025 |
| BARC bleeding 4, n (%) | - | - | - | - | - | - | - |
| BARC bleeding 5, n (%) | 1 (0.2) | 1 (0.4) | 0 (0) | 0.49 | 1 (0.6) | 0 (0) | 1.00 |

ACS, acute coronary syndrome; BARC, Bleeding Academic Research Consortium; LMWH, low-molecular weight heparin; MACCE, major adverse cardiac or cerebrovascular events.

What does this paper add?

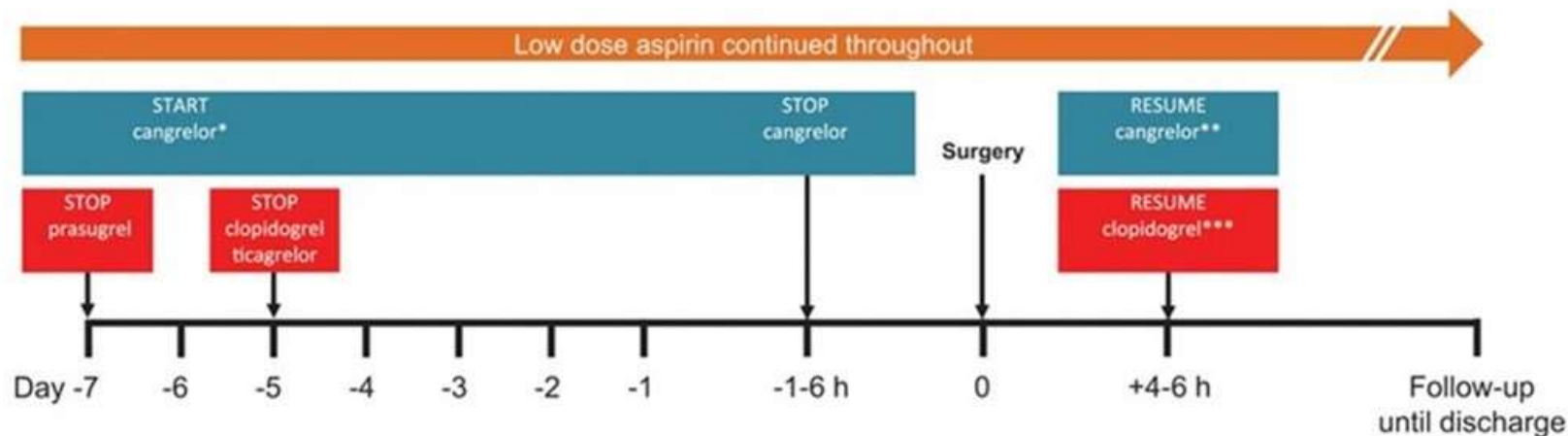
- Discontinuation of antiplatelet therapy and bridging with LMWH in stented patients on aspirin or dual antiplatelet therapy may be a detrimental practice.
- Compared with continuation of antiplatelet therapy, LMWH bridging was independently and consistently associated with a ≈ 10 - to 12-fold increased risk of MACCE compared with continuation of antiplatelet therapy (driven by a high risk of myocardial infarction) and a ≈ 2 -fold increased risk of BARC bleeding ≥ 2 (mostly type 3).

A

*Tirofiban: 0.1 mcg/Kg/min; If creatinine clearance <50 mL/min, adjust to 0.05 mcg/Kg/min. Eptifibatid: 2.0 mcg/Kg/min; If creatinine clearance is <50 mL/min, adjust to 1.0 mcg/Kg/min.

**If oral administration not possible

***With 300-600 mg loading dose, as soon as oral administration possible. Prasugrel or ticagrelor discouraged

B

*Initiate within 72 hours from P2Y₁₂ inhibitor discontinuation at a dose of 0.75 µg/Kg/min for a minimum of 48 hours and a maximum of 7 days.

**If oral administration not possible

***With 300-600 mg loading dose, as soon as oral administration possible. Prasugrel or ticagrelor discouraged

Stent Teknolojisinde Gelişmeler

- 1.jenerasyon (sirolimus, paclitaxel)
- 2.jenerasyon (zotarolimus, everolimus)
- 3.jenerasyon
 - Platform (cobalt-chromium, titanium, bioresorbable stent)
 - Polimer (polimer kütlesi az, biodegradable polimer, polimer-free)
 - İlaçlar
 - Biolimus, supralimus
 - Kısa salınım
 - Endotel hücrelerini davet eden antikorlar

Stent hastasında perioperatif MI

- Aynı veya başka damarda yerleşmiş perkütan koroner girişimde dokunulmamış stenotik lezyonlar
- Restenotik stentler
- Antiplatelet tedavini kesilmesi
- Antiplateletlerin idamesine rağmen stent trombozu
 - Yetersiz endotelizasyon
 - Artmış trombojenite
 - Post-MI
 - Kansere bağlı
 - Postoperatif dönemde antiplateletlerin yetersiz GIS absorpsiyonu

Kanama Riski

- Di Minno et al. 2009
 - ASA ile kan kaybı 2.5-20%, DAPT ile 30-50% artabilir
 - **Mortalitede kanamayla ilgili bir artış yok**
- Eberli et al. 2010
 - Cerrahi kanama riski ASA ile 20%, klopidogrel ile 50% artabilir

Preoperative antiplatelet use does not increase incidence of bleeding after major operations



David S. Strosberg, MD,* Todd Corbey, BS,* Jon C. Henry, MD,[‡] and Jean E. Starr, MD,[§] Columbus and Athens, OH, and Pittsburgh, PA

Surgery, 2016

Table III. Comparison of perioperative events between Groups A and B

| <i>Perioperative event*</i> | <i>Group A- clopidogrel withheld (n = 116)</i> | <i>Group B- clopidogrel given (n = 89)</i> | <i>P value</i> |
|--|--|--|----------------|
| Total patients who required preoperative platelet transfusions | 0 | 2 (2.2%) | .99 |
| Total patients who required perioperative transfusion | 34 (29.3%) | 34 (38.2%) | .23 |
| Number of packed red blood cell transfusions [†] (mean) | 2.65 | 2.53 | .81 |
| Estimated blood loss [‡] (mean) | 390.80 | 300.90 | .19 |
| Myocardial infarction | 3 (2.6%) | 1 | .63 |
| Cerebrovascular event | 1 | 2 (2.2%) | .58 |
| Acute lower extremity or visceral ischemia | 3 (2.6%) | 3 (3.4%) | .99 |
| Death within 30 days | 3 (2.6%) | 3 (3.4%) | .99 |

Outcomes of Laparoscopic Partial Nephrectomy in Patients Continuing Aspirin Therapy

David A. Leavitt, Mohamed Keheila,* Michael Siev, Paras H. Shah, Daniel M. Moreira, Arvin K. George, Simpa S. Salami, Michael J. Schwartz, Lee Richstone, Manish A. Vira and Louis R. Kavoussi

From the Department of Urology, Smith Institute for Urology, Hofstra North Shore LIJ School of Medicine, New Hyde Park, New York

Urology, 2016

J.

Postoperative complications

| | No. Overall (%) | No. on Aspirin (%) | No. off Aspirin (%) | p Value |
|-----------------------------|-----------------|--------------------|---------------------|---------|
| Total | 20 (20) | 3 (19) | 17 (20) | 1.00 |
| Clavien IIIa | 5 | 0 (0) | 5 | 0.59 |
| Clavien IIIb | 2 | 0 (0) | 2 | 1.00 |
| Clavien IVb | 3 | 1 (6) | 2 | 0.43 |
| Thromboembolic events | 1 | 0 (0) | 1 (1) | 1.00 |
| Readmission | 9 | 1 (6) | 8 (10) | 1.00 |
| Bleeding related | 8 | 1 (6) | 7 (8) | 1.00 |
| Transfusion | 6 | 2 (12) | 4 (5) | 0.25 |
| Angiography or embolization | 5 | 1 | 4 | 1.00 |
| Periop mortality | 0 (0) | 0 (0) | 0 (0) | 1.00 |

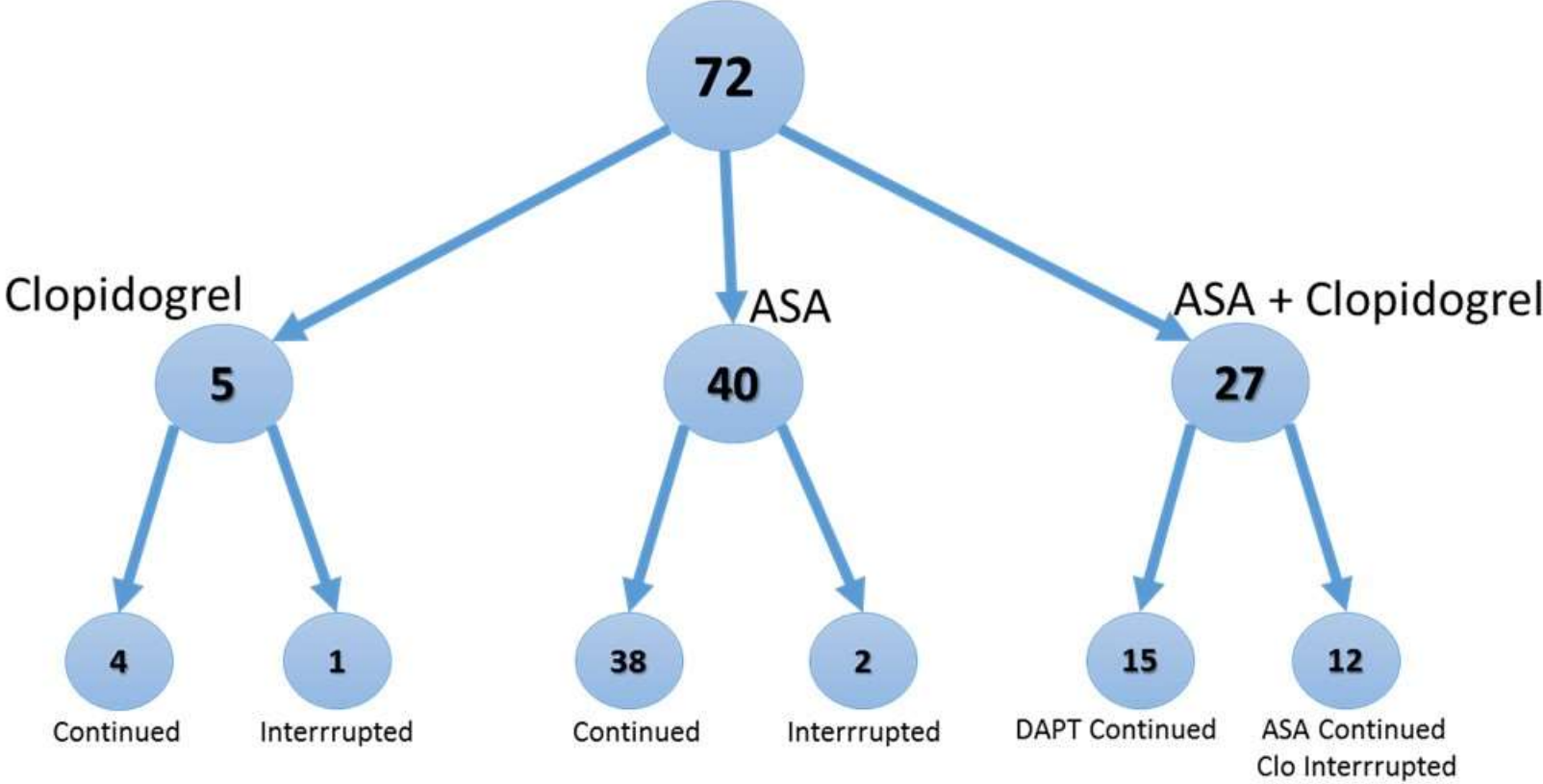
«Vulnerable period»

- Malignite-opere
 - PCI'den 1-3 ay sonra aktüel antiplatelet tedavi altında
- Diğer-hasta bazında karar
 - Elektif vakalar----- 1 yıl ertele
 - Yarı-elektif ----- PCI'den 6 ay sonra aktüel antiplatelet tedavi altında

«Vulnerable period» dışında

- Aktüel antiplatelet tedavi altında
- Kanama riski yüksekse
 - Kardioloji konsültasyonu düşük trombotik risk hakkında net bilgiler veriyorsa
 - DAPT---- ASA
 - Tek antiplatelet ajan ---- kes

Urologic Surgery



Interval between
PCI and surgery

| | | | | | | | | | | | |
|----------|---|----------|---|----------|----|----------|---|----------|----|----------|----|
| < 1 year | 2 | < 1 year | 0 | < 1 year | 10 | < 1 year | 0 | < 1 year | 10 | < 1 year | 1 |
| > 1 year | 2 | > 1 year | 1 | > 1 year | 28 | > 1 year | 2 | > 1 year | 5 | > 1 year | 11 |

69 hasta

| | |
|----------------------------------|----|
| • Sistoskopi-Bx | 8 |
| • TUR-mesane tm. | 22 |
| • TUR- prostat | 5 |
| • Açık/Lap radikal nefrektomi | 11 |
| • Açık/Lap parsiyel nefrektomi | 3 |
| • Radikal sistektomi | 8 |
| • Açık/Lap radikal prostatektomi | 10 |
| • Diğer | 2 |

Komplikasyonlar

- Mesane hematomu-reoperasyon

- TUR-T

DAPT

- TUR- T

Klopidogrel



Maç Nerede ?

Reoperasyon 1 Cerrah 0





Tromboz

Kanama