21. Göğüs Kalp Damar Anestezi ve Yoğun Bakım Derneği ULUSAL KONGRESİ

23 - 26 Nisan 2015
Perissia Otel - KAPADOKYA

www.gkda2015.com

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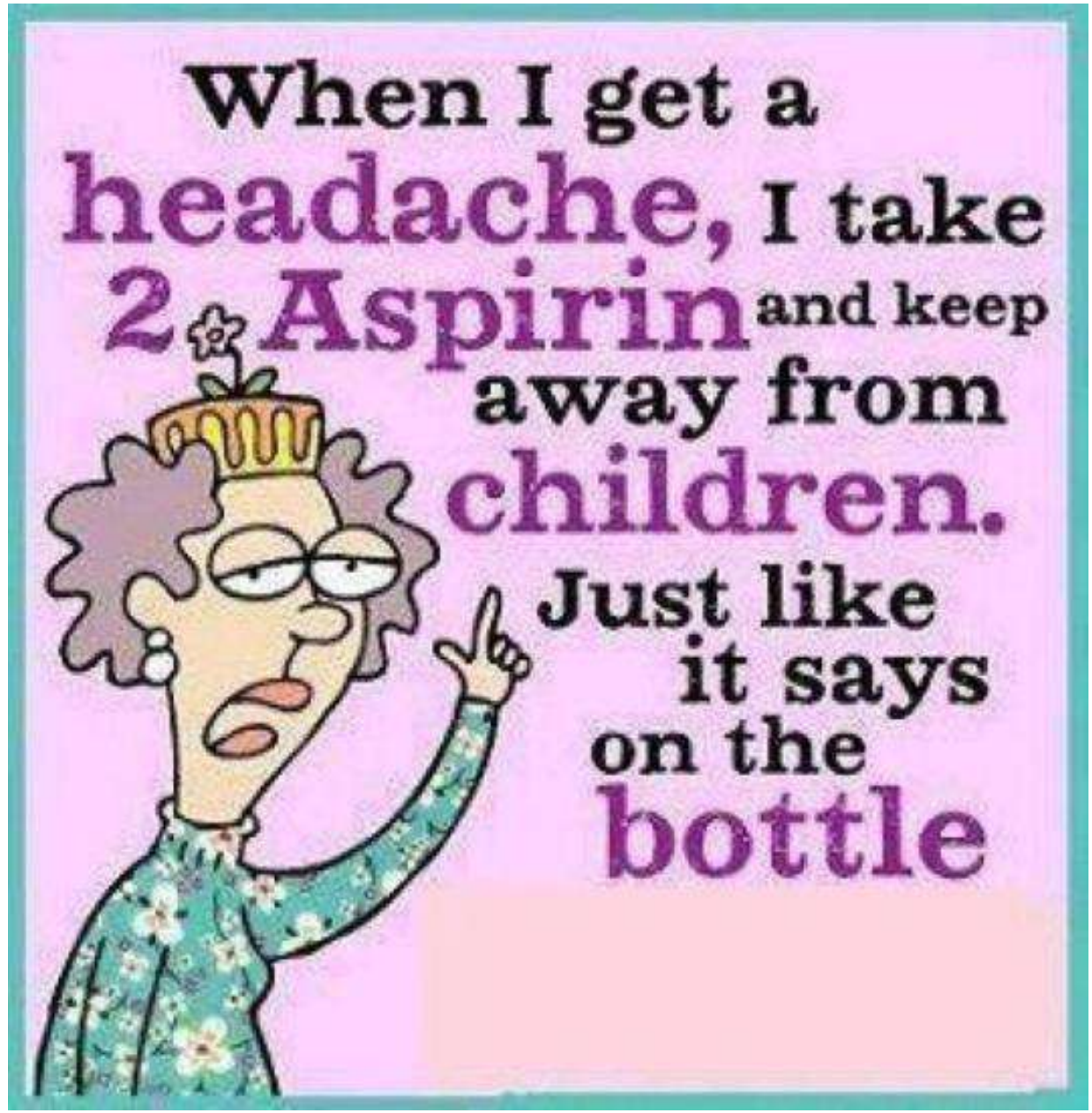
Disclosures

No financial disclosures

POISE investigator

...and...


When I get a
headache, I take
2 Aspirin and keep
away from
children.
Just like
it says
on the
bottle

Learning Objectives

Short history of aspirin

Antiplatelet drug – how does it work?

To know whether or not periop. administration of aspirin

- **improves outcome in all patients at cardiac risk**
- **improves outcome in subgroups of patients at risk**
- **worsens outcome (in some subgroups?)**

Aspirin – an old drug

Initially (only) **a drug against pain**

Who knows when it was discovered / invented?

The history of aspirin

THE NIGHT,
WHEN ASPIRIN
WAS INVENTED

true

The history of aspirin

- **Ancient peoples already knew salicylic acid** (from the bark of the willow tree) **and used it as a drug**

- **1859: Hermann Kolbe succeds to synthetize salicylacid chemically**

- **1897:Bayer chemicist Arthur Eichengrün and pharmacist Felix Hofmann develop acetylsalicylic acid: ASPIRIN**

➢ **An incredible success story begins**

Aspirin
–
Indications

Aspirin

–

Indications

How does aspirin “affect the heart”?

Aspirin is an “antiplatelet” drug

- **it irreversibly acetylates cyclooxygenase**
- inhibits the production of thromboxane A2
- platelet aggregation by adenosine and collagen ↓
- platelets exposed to aspirin have diminished aggregation in response to thrombogenic stimuli[1,2]

1 Lancet 1968;1:1431 2 Curr Ther Res 1978;23:194–199

How does aspirin “affect the heart”?

Aspirin is an “antiplatelet” drug

- **prevents thrombotic events**

Meta-analysis of 195 studies /135 000 high-risk patients

- **22% reduction of death rate from any vascular cause by aspirin administration**

1 Antithrombotic Trialists Collaboration. BMJ 2002;324:71–86

Aspirin can cut death rates

Does aspirin work in all populations?

Antiplatelet therapy with aspirin in patients with

- **Established CV disease** (secondary prevention)
- **Risk factors for CV disease** (primary prevention)
- **Coronary stents** to prevent restenosis + thrombosis
- **Bioprosthetic valves** to reduce thromboemboli

➢ **Scientific evidence in all groups?**

Evidence in favour of aspirin in

Secondary prevention: strong meta-analytic evidence[1]

- **AHA guideline**[2]**:**
  - **Patients with CAD, cerebrovascular D, PAVD should receive aspirin indefinitely unless the risk of bleeding outweighs the benefit**
  - **Patients with stents: dual antiplatelet therapy**
    - **≥6 weeks (bare-metal stent) ≥ 12 months (DES)**

1 Antithrombotic Trialists Collaboration. BMJ 2002;324:71–86

2 Circulation 2011;124:2458–73

Evidence in favour of aspirin in

Primary prevention: less robust evidence!

- **Position statement / consensus document[1]:**
  - **Aspirin therapy in patients with diabetes** (men >50, women >60) **who have ≥1 additional risk factor:** tobacco use, hypertension, hypercholesterolemia, albuminuria, or a significant family history of CV disease

*1 Position statement of the **American Diabetes Association**, a scientific statement of the **AHA**, and an expert consensus document of the **ACC** Foundation. Circulation 2010;121:2694–701*

Aspirin prevents thrombotic events

➢ Give aspirin to all surgical patients?

- **Prevention of thrombotic events**
- **Increased risk of bleeding**

Risk of bleeding –

Why not stop aspirin prior to surgery?

Surgery increases thrombotic risk

- **Inflammatory and hypercoaguable state**
- **Reduces fibrinolysis**
- **Unstable hemodynamics**

- **Pre-existing cv disease -> risk of myocardial infarction**
  - **Major periop. cardiac events in risk patients: 4%**
  - **Mortality of perioperative MI up to 25%!**

CMAJ 2005;173:627-34 (Review)

Prospective periop. studies on aspirin

- **Oscarsson et al**[1]
  - 210 pts at high cardiac risk
  - 75 mg aspirin vs. placebo 7d preop – 3 days postop
  - MACE ↓, bleeding complications ≅
- **STRATAGEM trial**[2]
  - 295 pts on aspirin for secondary prevention
  - MACE ≅, bleeding complications ≅

1 Br J Anaesth 2010;104:305–12

2 Br J Anaesth 2011;107:899–910

POISE-2 Trial[1]

"To determine the impact of low-dose aspirin on at-risk patients undergoing non-cardiac surgery"

- randomized controlled multicenter international double-blinded trial conducted from 2010 to 2013
- 10 010 patients undergoing noncardiac surgery
- Aspirin: 200 mg, then 100mg x 7d vs. placebo
- Initiation stratum and continuation stratum
- Primary outcome: composite of death + nonfatal MI at 30d

1 Devereaux PJ, et al; POISE-2 Investigators. Aspirin in patients undergoing noncardiac surgery. N Engl J Med 2014;370:1494–503

POISE-2 Trial

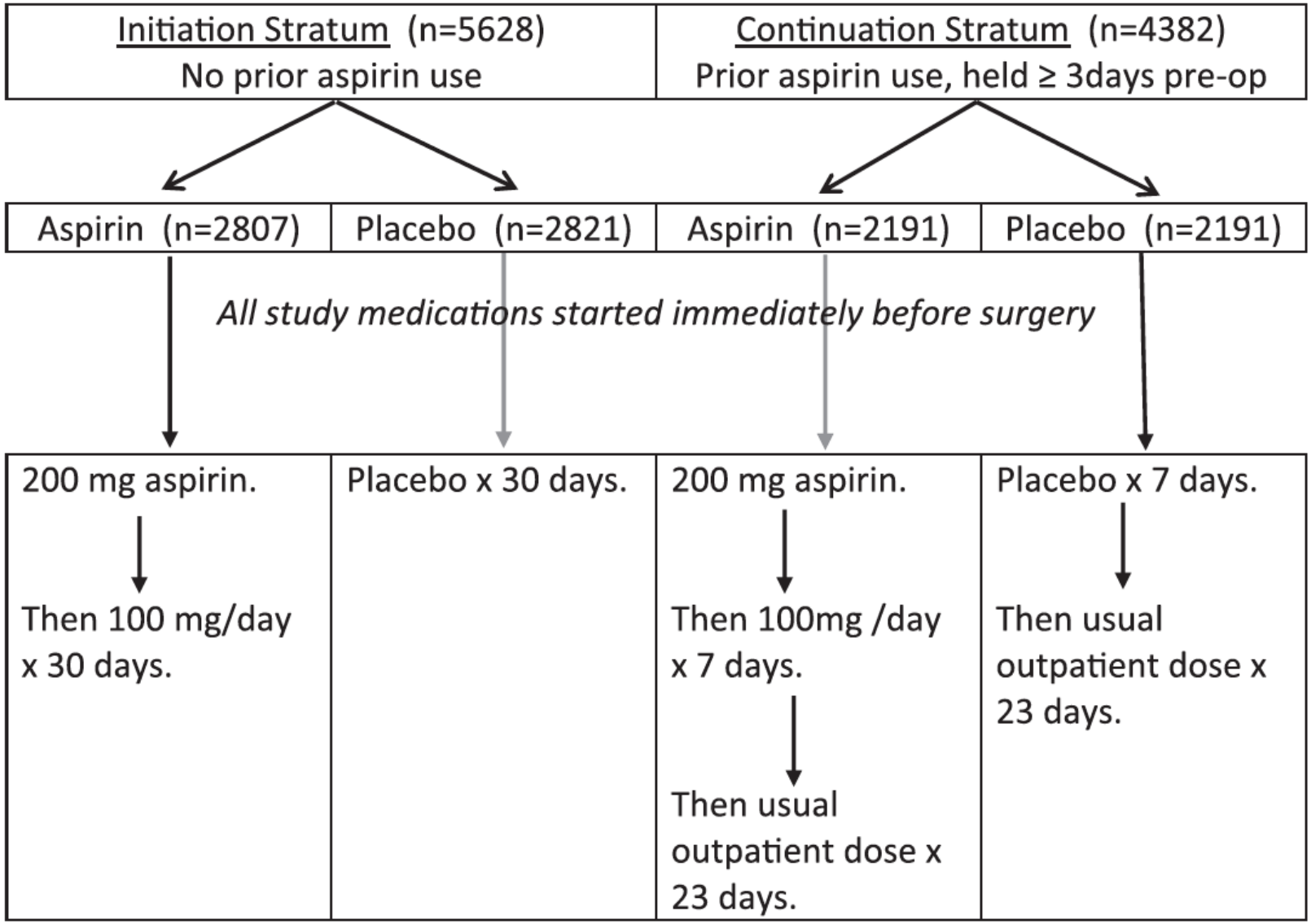


Table 2. Effects of Aspirin on 30-Day Outcomes.*

Outcome	Aspirin (N=4998)	Placebo (N=5012)	Ha	P Value
	no. (%)			
Primary composite outcome: death or nonfatal myocardial infarction	351 (7.0)			0.92
Secondary outcomes				
Death, nonfatal myocardial infarction, or nonfatal stroke			–1.13)	0.80
Death, nonfatal myocardial infarction cardiac revascularization, nonf pulmonary embolism, or deep venous thromb			0.99 (0.86–1.14)	0.90
Safety outcomes				
Life-thre	(1.7)	73 (1.5)	1.19 (0.88–1.63)	0.26
M	230 (4.6)	188 (3.8)	1.23 (1.01–1.49)	0.04

	87 (1.7)	73 (1.5)	1.19 (0.88–1.63)	0.26
	230 (4.6)	188 (3.8)	1.23 (1.01–1.49)	0.04
nportant hypotension	2143 (42.9)	2096 (41.8)	1.03 (0.97–1.09)	0.37
e	16 (0.3)	19 (0.4)	0.84 (0.43–1.64)	0.62
Congestive heart failure	44 (0.9)	38 (0.8)	1.16 (0.75–1.79)	0.50
Infection	488 (9.8)	495 (9.9)	0.99 (0.87–1.12)	0.86
Sepsis	243 (4.9)	258 (5.2)	0.94 (0.79–1.13)	0.52

the risk of continuing perioperative aspirin may be greater than the risk of cessation[1,2]

1 Devereaux PJ, et al; POISE-2 Investigators. N Engl J Med 2014;370:1494–503
2 Vaishnava P, Eagle KA. N Engl J Med 2014;370:1554–5 Editorial to POISE-2 Study

Aspirin cannot help preventing a heart attack without the risk of bleeding?

"An aspirin a day will help prevent a heart attack if you have it for lunch instead of a cheeseburger."

Limitations of the POISE-2 Trial

- Only 23% of patients had known CAD
- Only 36% of patients in the aspirin group fulfilled AHA guideline criteria for aspirin treatment for primary or secondary prevention
- Continuation stratum: indications for previous aspirin use unclear – how many fulfilled AHA guideline criteria for primary / secondary prevention?

➢ 2/3 of patients did not fulfil AHA guideline criteria for aspirin treatment and were included into POISE-2 because of high risk surgery (but only 5% vascular!)

➢ ***Patients at low risk for thrombotic complications***

Limitations of the POISE-2 Trial

- Patients at low risk for thrombotic complications
- Anticoagulation and antiplatelet treatment within 3d of sx
  - 65% prophylactic anticoagulation
  - 4% / 4.5% therapeutic anticoagulation
  - 1.2% P2Y12 inhibitors (clopidogrel, prasugrel, ticagrelor)
- Administration of NSAIDS in aspirin strata (9.5%)
  - Substrate competition: Inability of aspirin to access the receptor binding sites of the cyclooxygenase-1 enzyme
    - ➢ Possible cause for aspirin resistance

➢ ***Antithrombotic distinctions between groups attenuated***

Limitations of the POISE-2 Trial

- Major **bleeding** 4.6% vs. 3.8% (p=0.04)
- No differences in life-threatening bleeding and hypotension
- Post-hoc analysis: major + life-threatening bleeding postop
  - 1.2% increase in risk for composite until day 30 in aspirin group
  - Predictor of MI (hazard ratio 1.82 (1.40-2.36; p<0.001)
- Large meta-analysis[1] & prospective trial[2]: risks of bleeding non-significant with aspirin in non-closed space surgery
- Populations with high thrombotic risk excluded in POISE-2: carotid endarterectomy, recent coronary stents

1 J Intern Med 2005;257:399–414 *2 Br J Anaesth 2010;104:305–12*

➢ *POISE-2 cannot affirm that aspirin risk>benefit in high-risk pts*

Limitations of the POISE-2 Trial

- **DVT** (0.5% vs. 0.7%) and **PE** (0.7% vs. 0.6%) = similar

➢ POISE-2 was not powered to study these tertiary outcomes

- Pulmonary embolism prevention trial[1]
  - 17444 patients undergoing hip surgery
  - Aspirin vs. placebo preoperatively – day 35
  - PE risk ↓ 43%, symptomatic DVT risk ↓23% in aspirin group independent of heparin use

1 Lancet 2000;355:1295–302

Perioperative prevention of DVT & venous thromboembolism (VTE)

- **ACCP guidelines for prophylaxis of VTE[1] (1B)**
  - use of a single drug from the following list:

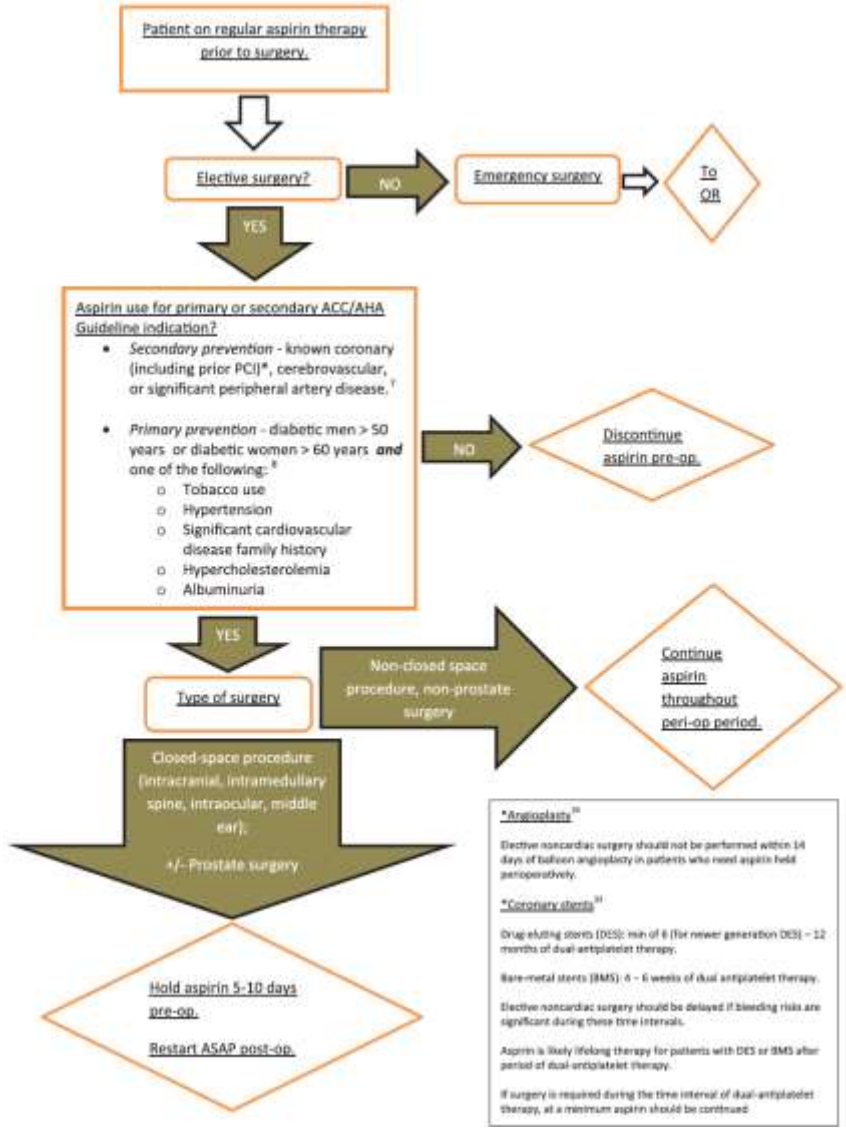
aspirin, LMW heparin, low-dose unfractionated heparin, fondaparinux, dabigatran, apixaban, and rivaroxaban

- **Secondary prophylaxis of VTE[2]**
  - High-risk: life-long anticoagulation
  - Moderate risk: aspirin

1 Chest 2012;141:e278S–325 *2 Circulation 2014;130:1031–3*

"To play it safe, I still take one aspirin every other day."

Algorithm for patients on aspirin presenting for surgery

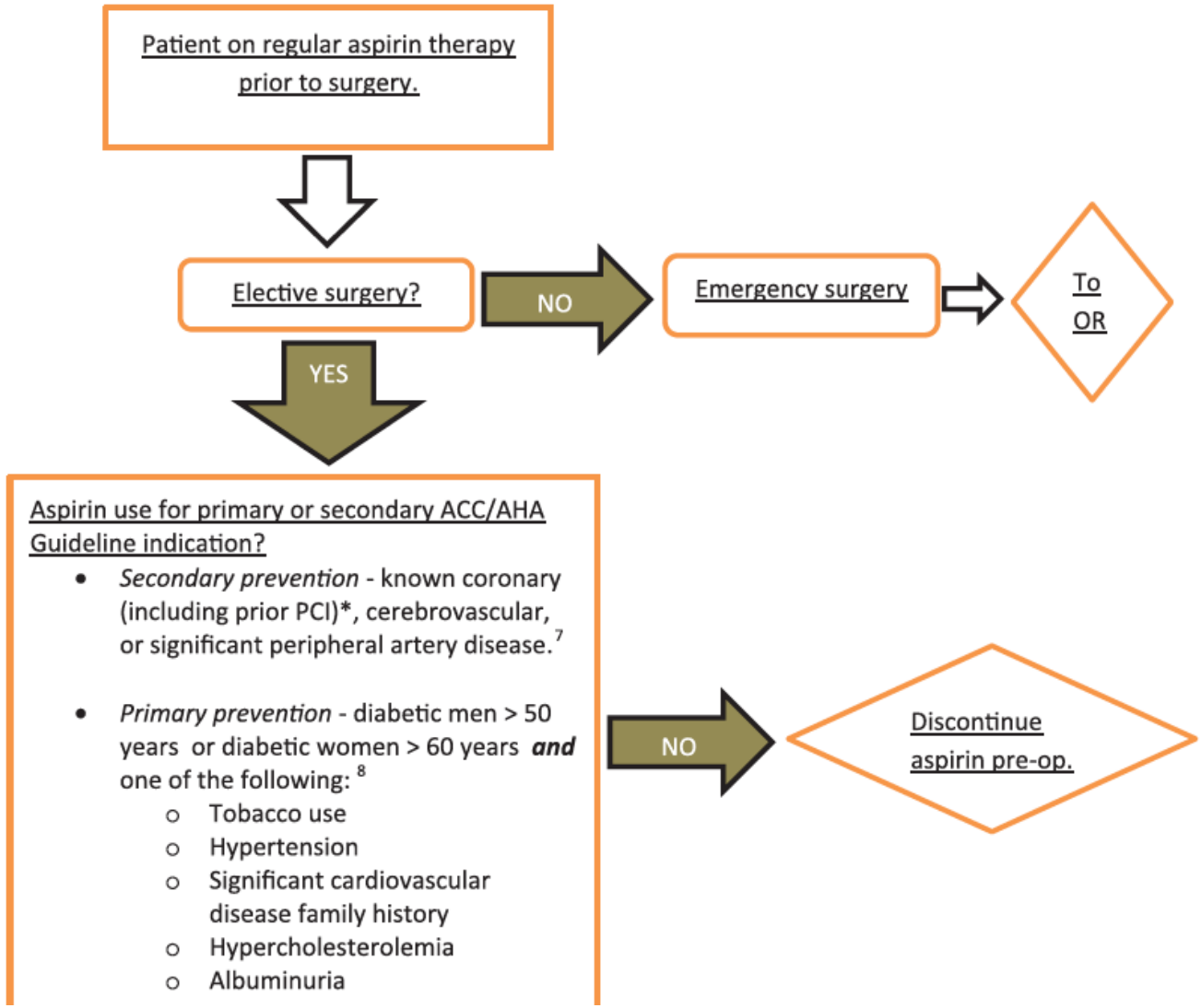


Perioperative Aspirin Management After POISE-2: Some Answers, but Questions Remain

Neal Stuart Gerstein, MD, FASE,* Michael Christopher Carey, MD,* Joaquin E. Cigarroa, MD,† and Peter M. Schulman, MD‡

(Anesth Analg 2015;120:570–5)

Algorithm for patients on aspirin presenting for surgery



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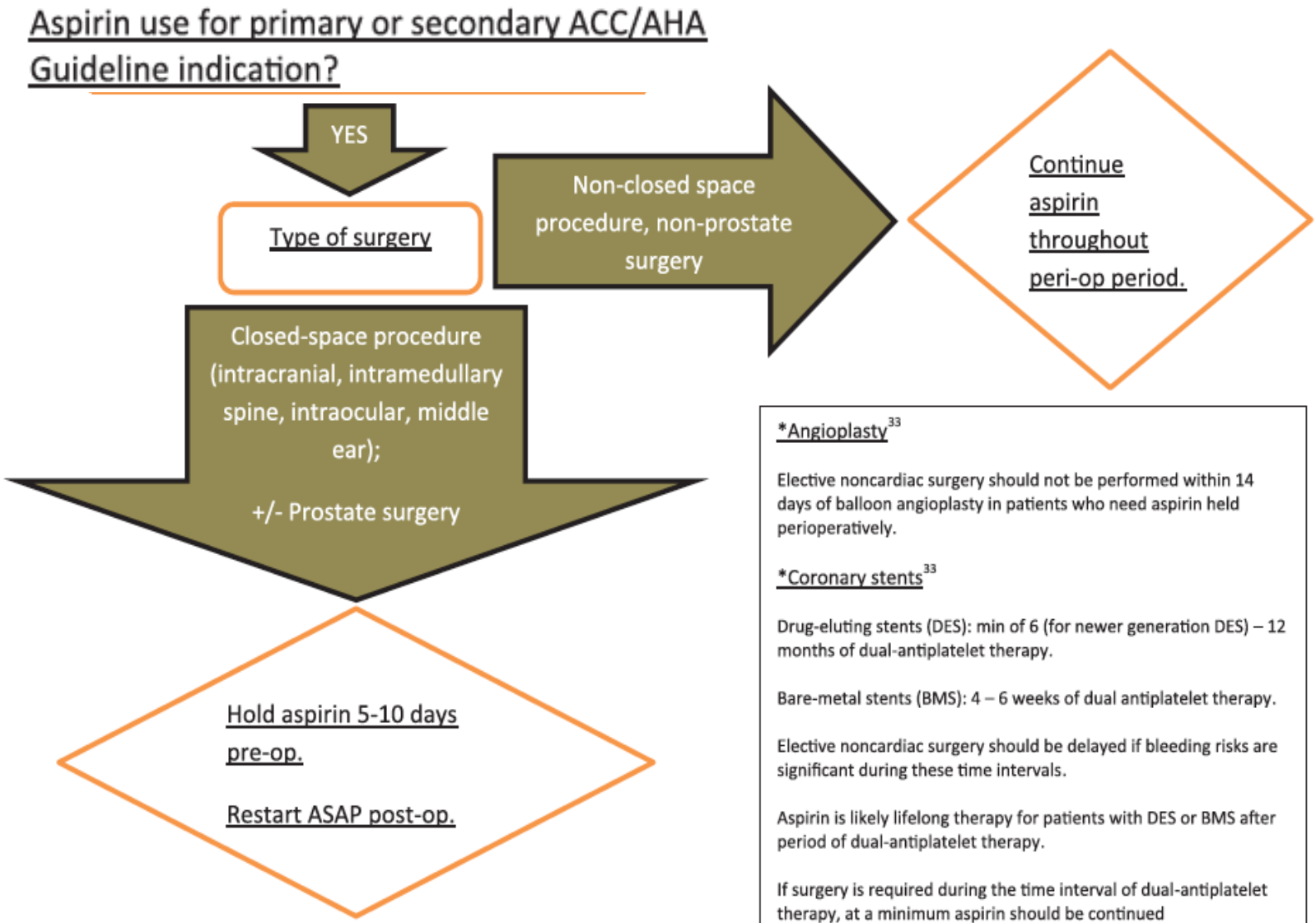

*Angioplasty[33]

Elective noncardiac surgery should not be performed within 14 days of balloon angioplasty in patients who need aspirin held perioperatively.

*Coronary stents[33]

Drug-eluting stents (DES): min of 6 (for newer generation DES) – 12 months of dual-antiplatelet therapy.

Bare-metal stents (BMS): 4 – 6 weeks of dual antiplatelet therapy.

Elective noncardiac surgery should be delayed if bleeding risks are significant during these time intervals.

Aspirin is likely lifelong therapy for patients with DES or BMS after period of dual-antiplatelet therapy.

If surgery is required during the time interval of dual-antiplatelet therapy, at a minimum aspirin should be continued

(Anesth Analg 2015;120:570–5)

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UNI BASEL

May 11th – 13th, 2016

Basel, Switzerland

With support from the City of Basel