Perioperative management of cardiac patients during non-cardiac surgery

Donat R. Spahn

Conflict-of-Interest

- **Consulting for B. Braun, CSL Behring, Vifor International**
- **ABC / ABC trauma faculty, managed by Thomson Physicians World GmbH (unrestricted educational grant - Novo Nordisk, CSL Behring, LFB Biomédicaments)**
- **In the past 5 years I received honoraria / travel support for occasional consulting / lecturing:**

Honoraria / travel support for occasional consulting / lecturing

Abbott	AMGEN	AstraZeneca
Baxter	B. Braun	Boehringer Ingelheim
Bristol-Myers-Squibb	CSL Behring	Curacyte
Ethicon Biosurgery	Fresenius	Galenica
GlaxoSmithKline	Janssen-Cilag	Merck Sharp & Dohme
Novo Nordisk	Octapharma	Organon
Oxygen Biotherapeutics	Photonics Healthcare	ratiopharm
Roche Diagnostics	Roche Pharma	Schering-Plough
Tem International	Verum Diagnostica	Vifor

European Heart Journal (2014) **35**, 2383–2431
doi:10.1093/eurheartj/ehu282

ESC/ESA GUIDELINES

2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management

The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA)

Authors/Task Force Members: Steen Dalby Kristensen* (Chairperson) (Denmark), Juhani Knuuti* (Chairperson) (Finland), Antti Saraste (Finland), Stefan Anker (Germany), Hans Erik Bøtker (Denmark), Stefan De Hert (Belgium), Ian Ford (UK), Jose Ramón Gonzalez-Juanatey (Spain), Bulent Gorenek (Turkey), Guy Robert Heyndrickx (Belgium), Andreas Hoeft (Germany), Kurt Huber (Austria), Bernard Iung (France), Keld Per Kjeldsen (Denmark), Dan Longrois (France), Thomas F. Lüscher (Switzerland), Luc Pierard (Belgium), Stuart Pocock (UK), Susanna Price (UK), Marco Roffi (Switzerland), Per Anton Sirnes (Norway), Miguel Sousa-Uva (Portugal), Vasilis Voudris (Greece), Christian Funck-Brentano (France).

Kristensen S. D. et al., Eur Heart J (2014) 35: 2383

Magnitude of the problem

- Europe: 19 Mio of major surgery annually
- 30% (5.7 Mio) extensive surgical procedures in patients with cardio-vascular risk factors
- Overall complication rate = approximately 10%
- 42% of complications are cardiac complications
- Europe: 167’00 cardiac complications, of which 19’000 are life-threatening
- Number of surgeries is expected to grow by 25% by 2020

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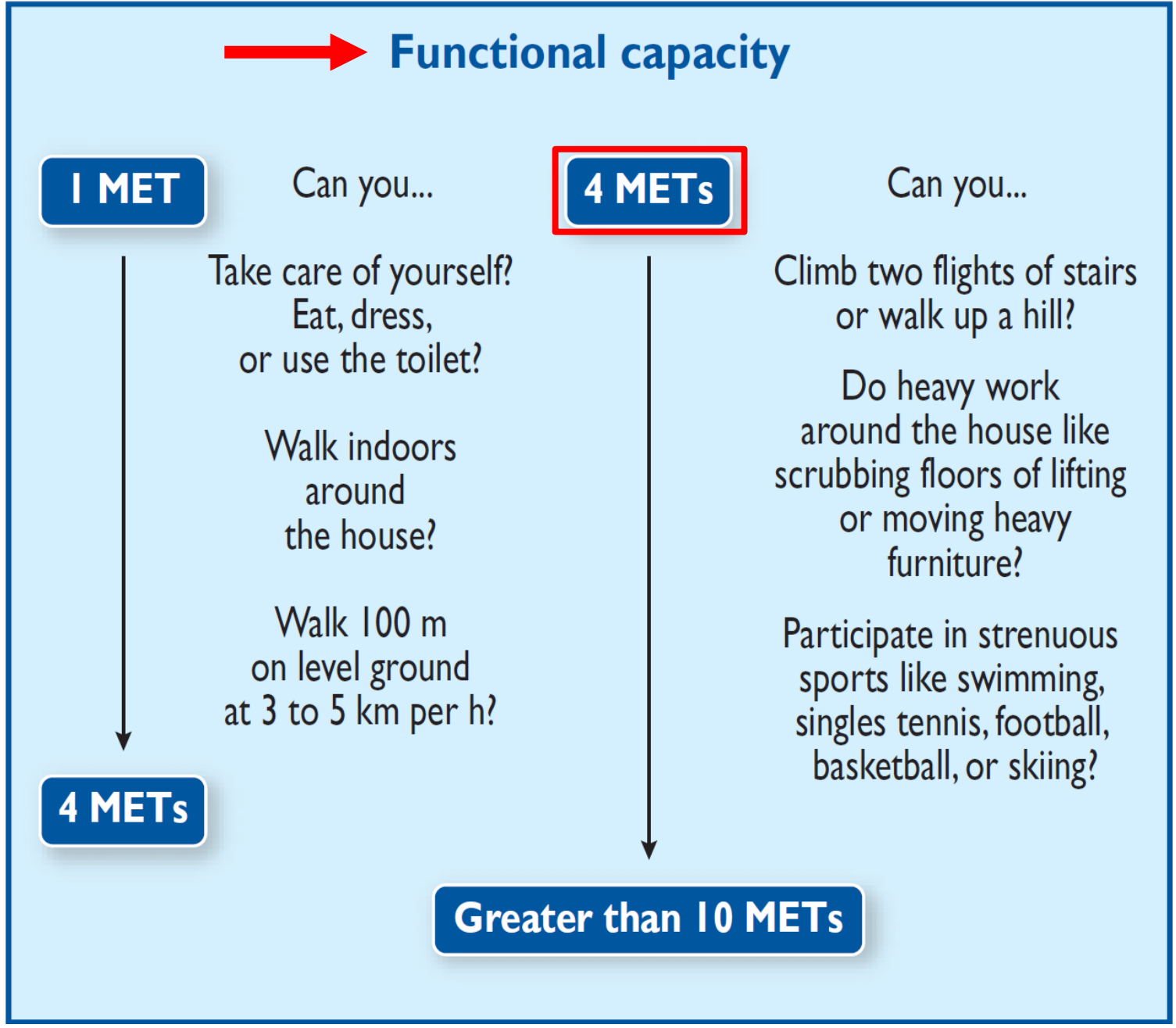
Preoperative evaluation and management



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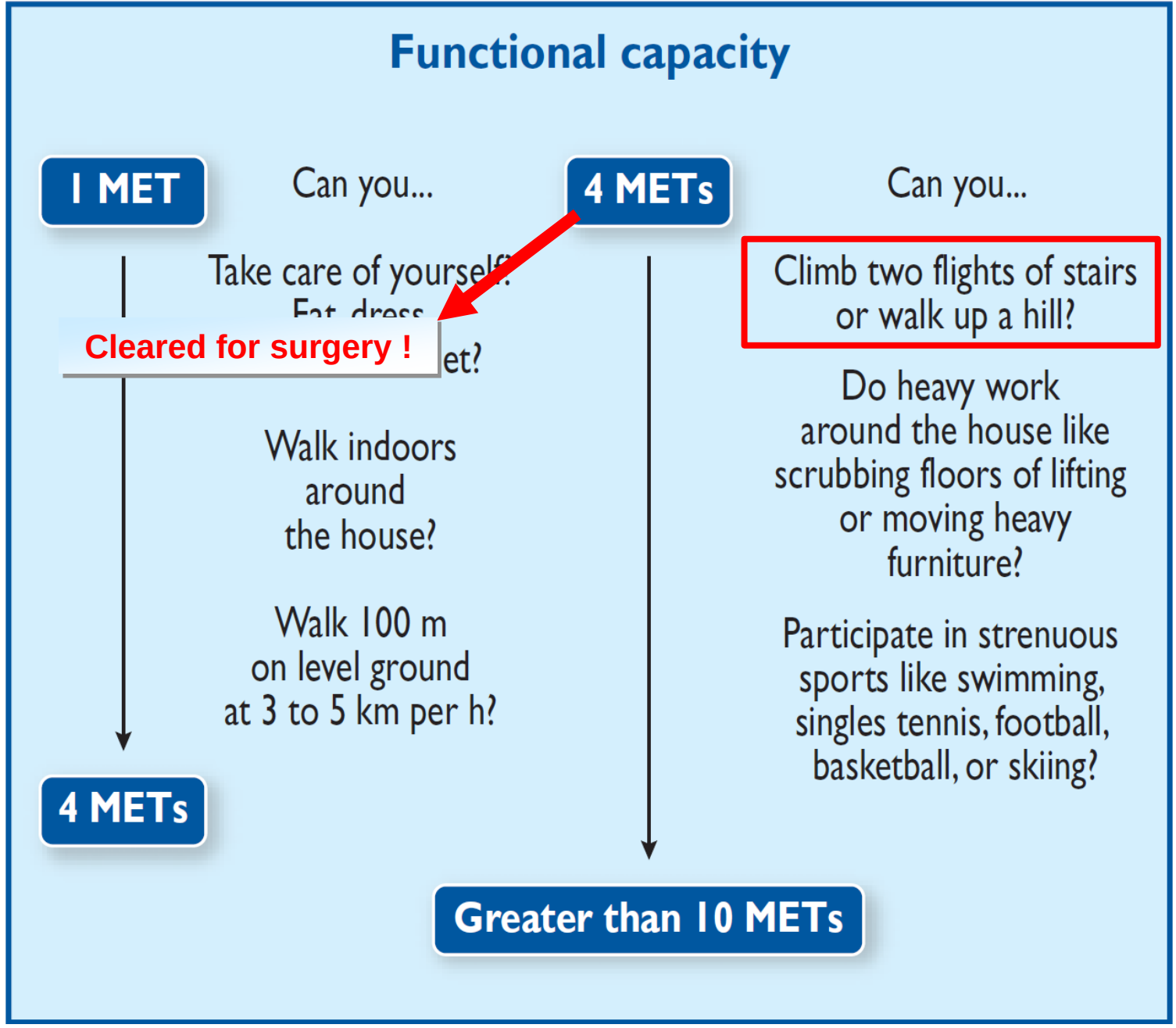

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Recommendations on routine pre-operative ECG

Recommendations	Class[a]	Level[b]	Ref.[c]
Pre-operative ECG is recommended for patients who have risk factor(s)[d] and are scheduled for intermediate- or high-risk surgery.	I	C	57

- Ischaemic heart disease (angina pectoris and/or previous myocardial infarction[a])
- Heart failure
- Stroke or transient ischaemic attack
- Renal dysfunction (serum creatinine >170 µmol/L or 2 mg/dL or a creatinine clearance of <60 mL/min/1.73 m^2)
- Diabetes mellitus requiring insulin therapy

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Recommendations on imaging stress testing before surgery in asymptomatic patients

1. Very few patients

2. Only if new information can be expected that

- can be treated preoperatively

- without interfering with the necessary surgery

Which of the high risk surgeries can wait 3-12 months ?

Recommendations	Class[a]	Level[b]
Imaging stress testing is recommended before high-risk surgery in patients with more than two clinical risk factors and poor functional capacity (<4 METs).[c]	I	C
Imaging stress testing may be consid before high- or intermediate-risk surgery in patients with one or two clinical risk factors and poor functio capacity (<4 METs).[c]		
Imaging stress testing is not recommended before low-risk surge regardless of the patient's clinical ris		

High-risk: > 5%

- Aortic and major vascular surgery
- Open lower limb revascularization or amputation or thromboembolectomy
- Duodeno-pancreatic surgery
- Liver resection, bile duct surgery
- Oesophagectomy
- Repair of perforated bowel
- Adrenal resection
- Total cystectomy
- Pneumonectomy
- Pulmonary or liver transplant

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Recommendations on pre-operative coronary angiography

What can the (therapeutic) consequences be ?
Patient / Surgery

Recommendations	Class[a]	Level[b]	Ref.[c]
Indications for pre-operative coronary angiography and revascularization are similar to those for the non-surgical setting.	I	C	56
Pre-operative angiography is not recommended in cardiac-stable patients undergoing ~~low-risk~~ surgery.	III	C	

Personal view

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Recommendations on beta-blockers

Personal view

Recommendations	Class[a]	Level[b]	Ref.[c]
Peri-operative continuation of beta-blockers is recommended in patients currently receiving this medication.	I	B	96–99

Patients with a clear indication for beta-blocker treatment are on beta-blockers normally in (most countries) in Europe

Initiation of peri-operative high-dose beta-blockers without titration is not recommended.	III	B	78
Pre-operative initiation of beta-blockers is not recommended in patients scheduled for ~~low-risk~~ surgery.	III	B	86,97

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Recommendations for prophylactic revascularization in stable/asymptomatic patients

Recommendations	Class[a]	Level[b]	Ref.[c]
Performance of myocardial revascularization is recommended according to the applicable guidelines for management in stable coronary artery disease.	I	B	56
Late revascularization after successful non-cardiac surgery should be considered, in accordance with ESC Guidelines on stable coronary artery disease.	I	C	
Prophylactic myocardial revascularization before high-risk surgery may be considered, depending on the extent of a stress-induced perfusion defect.	IIb	B	147
Routine prophylactic myocardial revascularization before ~~low- and intermediate-risk~~ surgery in patients with proven IHD is not recommended.	III	B	152

All surgery !

Which of the high risk surgeries can wait 3-12 months ?

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Perioperative drug management

- **Continue established treatment**
  - ➔ **Beta-blockers**
  - ➔ **Statins**
  - ➔ **Anti-hypertensive drugs**
  - ➔ **Aspirin (99% of patients)**
  - ➔ **Oral anti-arrhythmic drugs**
- **Drugs newly introduced preoperatively**
  - ➔ **Statins ?**
- **Short term interruption +/- bridging**
  - ➔ **Dual platelet inhibition**
  - ➔ **Oral anticoagulants (VKA, anti Xa, anti IIa)**

Next speaker, Dr. Binder

Choice of type of anesthesia / anesthetics

Choice of type of anesthesia / anesthetics

- **Feel free**
  - ➔ **Locoregional**
  - ➔ **Neuraxial (spinal, epidural)**
  - ➔ **General**
  - ➔ **Combined**
  - ➔ **Choice of anesthetic drugs**

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  - ➔ General
  - ➔ Combined
  - ➔ Choice of anesthetic drugs
- **As cardiologist, do not influence the patient in his choice**
- **The “best” anesthesia is the one with which the anesthetist feels comfortable with for the planned procedure**
  - ➔ Specific requirement for specific types of surgery
  - ➔ Specifics due to oral anticoagulants (VKA, anti Xa, anti IIa)

General vs. neuraxial anesthesia

Recommendations on anaesthesia

Recommendations	Class[a]	Level[b]	Ref.[c]
Patients with high cardiac and surgical risk should be considered for goal-directed therapy. **Fluid therapy**	IIa	B	261–264
The measurement of natriuretic peptides and high-sensitivity troponin after surgery may be considered in high-risk patients to improve risk stratification. **Pre- and postoperative strategy**	IIb	B	3,55,266, 268,272
Neuraxial anaesthesia (alone), in the absence of contra-indications and after estimation of the risk–benefit ratio, reduces the risk of peri-operative mortality and morbidity compared with general anaesthesia and may be considered. **Highly conditional**	IIb	B	10,252–257

Kristensen S. D. et al., Eur Heart J (2014) 35: 2383

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	Type	Comparison	Year of surgery / publication	N
Body, 1996	RCT	GA, Sp, E in peripheral vascular surgery	Year of surgery unknown	423
Rigg, 2002	RCT	GA ± E in major GI surgery	1995 - 2001	915
Rogers, 2000	Systemic review	Many types of surgeries	Published before 1997	9559
Mauermann, 2006	Meta-Analysis	Hip arthroplasty	Published 1977 - 2003	576
Wu, 2006	Random sample Medicare	Open colectomy	1997 - 2001	12’817
Memtsoudis, 2013	Hospital data base	Hip and knee arthroplasty	2006 - 2010	528’495
Guay, 2014	Review of Cochrande analyses			

	Type	Finding
Body, 1996	RCT	Mortality: NS Complications: Trend towards less in GA
Rigg, 2002	RCT	Mortality: NS Complications 7 of 8 types: NS Less pulmonary complications
Rogers, 2000	Systemic review	Death: -30% ⬇ in neuraxial anesthesia Less DVT, PE, pulmonary complications
Mauermann, 2006	Meta-Analysis	Less DVT in neuraxial anesthesia
Wu, 2006	Random sample Medicare	Death: -45% ⬇ in neuraxial anesthesia
Memtsoudis, 2013	Hospital data base	Mortality: Highest in GA Multivariate: Mortality ⬆ only in knee arthroplasty
Guay, 2014	Review of Cochrande analyses	

Table 2. Summary of New Findings

Neuraxial blockade (GA) compared with general anesthesia (GA) for perioperative mortality, myocardial infarction or chest infection

Patient or population: Patients with perioperative mortality
Settings: In hospital or ambulatory surgery
Intervention: Neuraxial blockade (GA)
Comparison: General anesthesia (GA)

Outcomes	Illustrative comparative risks[a] (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk General anesthesia (GA)	Corresponding risk Neuraxial blockade (GA)			
RA versus GA: mortality—Follow-up: 30 days	Study population		RR 0.71 (0.53–0.94)	3006 (20 studies)	⊕⊕⊕⊖ moderate[b]
	79 per 1000	56 per 1000 (42 –74)			
	Low-risk population				
	20 per 1000	14 per 1000 (11–19)			
	High-risk population				
	100 per 1000	71 per 1000 (53–94)			
RA versus GA: myocardial infarction—Follow-up: 30 days	Study population		RR 1.17 (0.57–2.37)	849 (6 studies)	⊕⊕⊕⊖ moderate[b]
	34 per 1000	40 per 1000 (19–81)			
	Low-risk population				
	20 per 1000	23 per 1000 (11–47)			
	High-risk population				
	60 per 1000	70 per 1000 (34–142)			
RA versus GA: pneumonia—Follow-up: 30 days	Study population		RR 0.45 (0.26–0.79)	400 (5 studies[c])	⊕⊕⊕⊖ moderate[b,d,e]
	167 per 1000	75 per 1000 (43–132)			
	Low-risk population				
	40 per 1000	18 per 1000 (10–32)			
	High-risk population				
	200 per 1000	90 per 1000 (52–158)			

Blinding problems

Blinding problems

Blinding problems

Guay J. et al., Anesth Analg (2014) 119: 716

Choice of type of anesthesia / anesthetics

- **Feel free**
  - ➔ Locoregional
  - ➔ Neuraxial (spinal, epidural)
  - ➔ General
  - ➔ Combined
  - ➔ Choice of anesthetic drugs
- **As cardiologist, do not influence the patient in his choice**
- **The “best” anesthesia is the one with which the anesthetist feels comfortable with for the planned procedure**
  - ➔ Specific requirement for specific types of surgery
  - ➔ Specifics due to oral anticoagulants (VKA, anti Xa, anti IIa)

British Journal of Anaesthesia **111** (6): 886–96 (2013)
Advance Access publication 12 July 2013 · doi:10.1093/bja/aet231

BJA

Anaesthetic drugs and survival: a Bayesian network meta-analysis of randomized trials in cardiac surgery

G. Landoni[1*], T. Greco[1], G. Biondi-Zoccai[2], C. Nigro Neto[3,4], D. Febres[1], M. Pintaudi[1], L. Pasin[1], L. Cabrini[1], G. Finco[5] and A. Zangrillo[1]

- **Meta-Analysis of 38 RCTs undergoing cardiac surgery**
- **Outcome**
  - ➔ **Effect of volatile anesthetic on mortality**
  - ➔ **Effect of sevoflurane / desflurane specifically**

Landoni G. et al., Br J Anaesth (2013) 111: 886

	Number of included studies	Events in the volatile group	Events in the TIVA group	OR (all in favour of volatile agents)	95% CI	*P*-value for effect
Mortality						
Overall analysis	35	25/1994 (1.3%)	43/1648 (2.6%)	0.51	0.33–0.81	0.004
Sensitivity analysis on mortality						
Low risk of bias studies	18	17/1380 (1.2%)	32/998 (3.2%)	0.42	0.24–0.73	0.002
Without the largest study (6)	34	12/1725 (0.7%)	25/1503 (1.7%)	0.63	0.36–1.11	0.11
More than 100 patients	16	22/1590 (1.4%)	39/1309 (3.0%)	0.43	0.25–0.72	0.002
CABG surgery studies	28	22/1746 (1.3%)	39/1402 (2.8%)	0.48	0.30–0.78	0.003
CPB-CABG surgery	22	21/1597 (1.3%)	37/1259 (2.9%)	0.45	0.27–0.75	0.002
OPCABG surgery	6	1/149 (0.7%)	2/143 (1.4%)	0.83	0.19–3.74	0.8
Non-CABG surgery	7	3/248(1.2%)	4/246 (1.6%)	0.82	0.23–2.89	0.8
Myocardial infarction	27	44/1879 (2.3%)	74/1560 (4.7%)	0.56	0.38–0.82	0.003
Inotropes use	21	309/1186 (26%)	426/1115 (38%)	0.42	0.31–0.59	<0.001

Landoni G. et al., Br J Anaesth (2013) 111: 886

Contrast	Volatile agents *vs* TIVA, longest follow-up	
	OR	95% credible interval
Sevoflurane *vs* TIVA	0.31†	0.14–0.64
Desflurane *vs* TIVA	0.43†	0.21–0.82
Isoflurane *vs* TIVA	0.42	0.15–1.09
Sevoflurane *vs* desflurane*	0.74	0.27–2.01
Sevoflurane *vs* isoflurane*	0.76	0.22–2.60
Desflurane *vs* isoflurane*	1.03	0.31–3.38

Landoni G. et al., Br J Anaesth (2013) 111: 886

Randomized Comparison of Sevoflurane Versus Propofol to Reduce Perioperative Myocardial Ischemia in Patients Undergoing Noncardiac Surgery

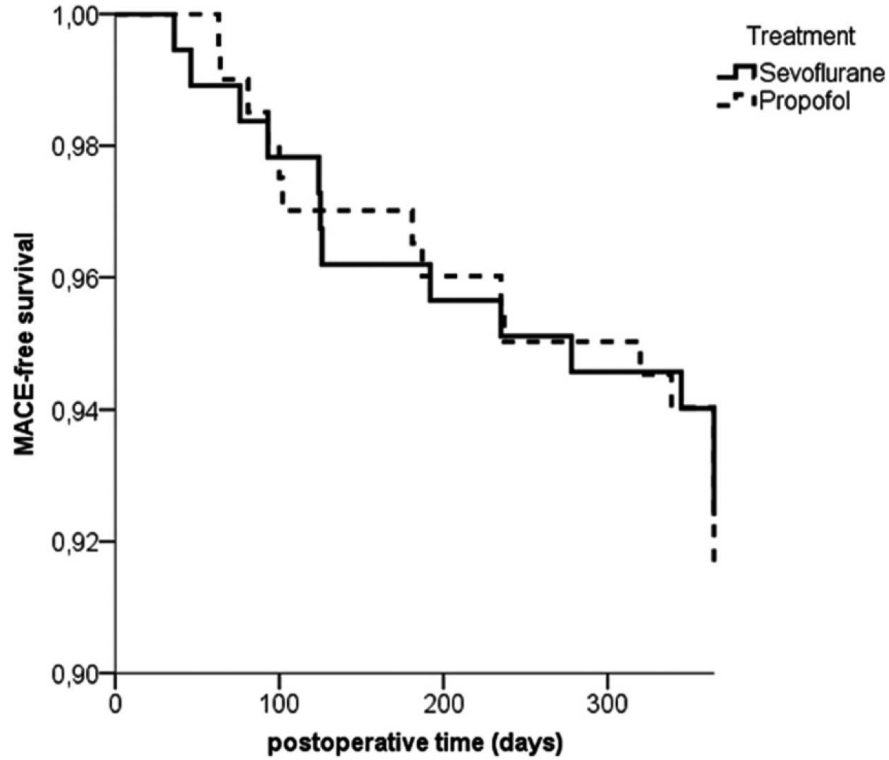
- RCT in 385 patients undergoing non-cardiac surgery (major general, major orthopedic and major vascular)
- Randomized to sevoflurane vs. propofol anesthesia
- Outcome
  - ➔ Troponin T (48h)
  - ➔ NT-proBNP (48h)
  - ➔ Major adverse events at 6 and 12 months

Lurati Buse G. A. L. et al., Circulation (2012) 126: 2696

Table 2. Study End Points and 12-Month Outcome by Treatment

	Sevoflurane (n=184)	Propofol (n=201)	RR or HR (95% CI)
Primary end point			
Myocardial ischemia (cECG and troponin)	75 (40.8)	81 (40.3)	RR=1.01 (0.78–1.30)
Secondary end points			
Myocardial ischemia on cECG*	41 (36.3)	36 (28.1)	RR=1.29 (0.87–1.91)
Troponin T elevation	46 (25.0)	57 (28.4)	RR=0.88 (0.62–1.25)
Myocardial ischemia or any Q-wave development	85 (46.2)	94 (46.8)	RR=0.99 (0.79–1.24)
Any Q-wave development (Minnesota codes I1–3)	17 (9.2)	18 (9.0)	RR=1.03 (0.52–2.0)
Q-wave infarction	1 (0.5)	1 (0.5)	RR=1.09 (0.03–39.8)
NT-proBNP, postoperative day 1, median (Q1–Q3), pg/mL	526 (257–1031.5)	559 (238–1234.5)	*P*=0.709
NT-proBNP, postoperative day 2, median (Q1–Q3), pg/mL	932.5 (450.5–1670.5)	928.5 (417.75–2068.5)	*P*=0.766
12-Month outcomes			
MACE	14 (7.6)	17 (8.5)	HR=0.90 (0.44–1.83)
Cardiac mortality	5 (2.7)	5 (2.5)	HR=1.09 (0.32–3.77)
All-cause mortality	25 (13.6)	23 (11.4)	HR=1.19 (0.67–2.09)

Lurati Buse G. A. L. et al., Circulation (2012) 126: 2696



	(n=184)	(n=201)	*P*
Postoperative delirium	21 (11.4)	29 (14.4)	0.379
PONV day 1	29 (15.8)	18 (8.9)	0.042
PONV day 2	17 (9.2)	15 (7.5)	0.544
NRS, median (Q1–Q3), day 1	7 (5–8)	7 (5–8)	0.173
NRS, median (Q1–Q3), day 2	7 (5–8)	7 (5–8)	0.734
NRS, median (Q1–Q3), day 7	8 (6–9)	7 (5–9)	0.122

Lurati Buse G. A. L. et al., Circulation (2012) 126: 2696

Intraoperative management

- **Monitoring**
  - ➔ **ECG, SaO2, temperature, endtidal CO2**
  - ➔ **Arterial catheter - frequently (volemia, BP control)**
  - ➔ **Central venous catheter – from time to time (postop need, catecholamines)**
  - ➔ **Pulmonary artery catheter – nearly never (PA hypertension)**
  - ➔ **TEE – rarely, if so, mostly due to unexplained hemodynamic difficulties**
- **Choice of anesthesia technique (general vs. neuraxial) free**
- **Choice of anesthetics for general anesthesia free**

Postoperative management

- **Site of treatment – plan ahead**
  - ➔ **PACU (all)**
  - ➔ **Intermediate Care Unit (primarily or after PACU)**
  - ➔ **Intensive Care Unit (selected cases after special operations, usually intubated and ventilated patients)**
- **Postoperative assessment is key for success**
  - ➔ **Hemodynamic and pulmonary stability ?**
  - ➔ **Drugs / procedures necessary for hemodynamic and pulmonary stability ?**
  - ➔ **Bleeding, coagulation ?**
  - ➔ **Timing for postoperative start of anti-coagulants and (second platelet inhibitor)**
- **Postoperative pain management – plan ahead**

Conclusion

- **Preoperative evaluation / pre-treatment**
  - ➔ **ESC / ESA Guidelines are very helpful**
  - ➔ **Be maximally restrictive in preoperative interventions to avoid interference with necessary surgery (plus costs !)**
- **Maintain most all drugs**
  - ➔ **Interruption of second platelet inhibitor (± bridging)**
  - ➔ **Interruption of anticoagulants (no bridging except VKA)**
- **Choice of anesthesia / anesthetics**
  - ➔ **Feel free**
- **Postoperative care**
  - ➔ **Plan ahead**
  - ➔ **Postoperative evaluation is to be decisive for further treatment (including site – ICU, intermediate care unit, ward)**

SGAR SSAR

Schweizerische Gesellschaft
für Anästhesiologie und Reanimation

Société Suisse d'Anesthésiologie et de Réanimation
Società Svizzera di Anestesiologia e Rianimazione

Informationen zu Medikamenten

Anwendung von Rivaroxaban - Guidelines der Expertengruppe «Rivaroxaban and anesthesiology» (Version November 2013)

Anwendung von Rivaroxaban - Guidelines der Expertengruppe «Rivaroxaban and anesthesiology» - Kurzversion (Version November 2013)

Anwendung von Rivaroxaban - Protokoll der wichtigsten inhaltlichen Anpassungen

Fondaparinux: Guidelines für die Anästhesiologie

Apixaban Guidelines

Anwendung von Ticagrelor im perioperativen Setting

Anwendung von Dabigatran in der Anästhesiologie

18.03.2014

Arbeitsplatz-basiertes Assessment

Vom SIWF/FMH aus müssen ab dem 1.1.2015 alle Fachdisziplinen für die Assistenten das...

10.03.2014

Fachexamen 2014/2015: Formulare sind aufgeschaltet

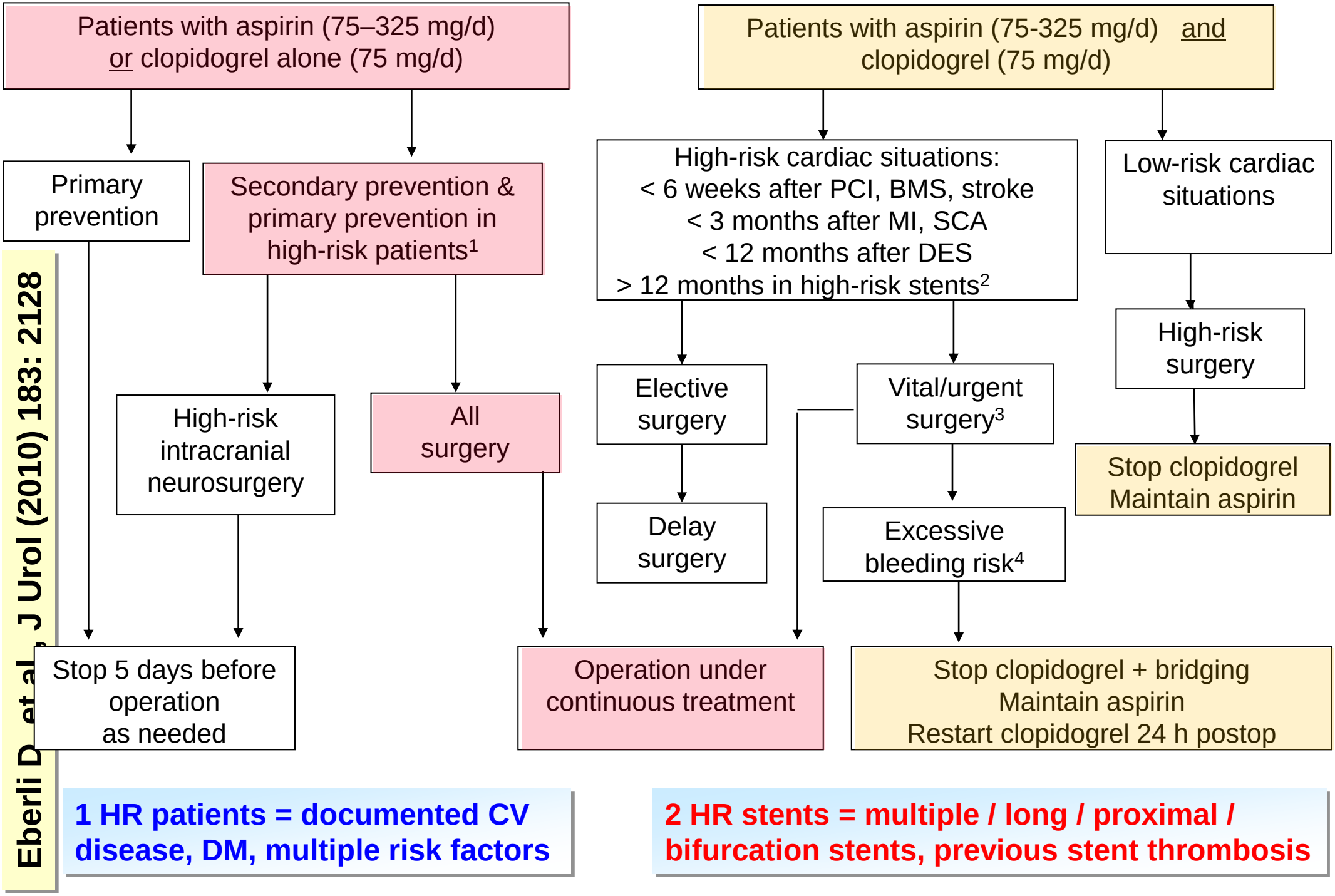
Link zum Formular

Weitere News...

Bridging

- Continue ASS (not the day of operation)
- Stop ADP receptor antagonists:
  - ➔ Clopidogrel: 5 days prior to the operation
  - ➔ Prasugrel: 7 days prior to the operation
  - ➔ Ticagrelor: 5 days prior to the operation
- Start GPIIb/IIIa antagonist 3 days prior to the operation
  - ➔ Tirofiban (Aggrastat®)
  - ➔ Eptifibatid (Integrilin®)
- Stop GPIIb/IIIa antagonist 22:00 the evening before the operation
- Start ADP receptor antagonists within 24h postop. (no loading dose)

Broad L. et al., Br J Anaesth (2007) 98: 19
Price M. J. et al. J Am Coll Cardiol (2012) 59: 2338


Patients with aspirin (75–325 mg/d) or clopidogrel alone (75 mg/d)
Patients with aspirin (75-325 mg/d) and clopidogrel (75 mg/d)
Primary prevention
Secondary prevention & primary prevention in high-risk patients[1]
High-risk cardiac situations:
< 6 weeks after PCI, BMS, stroke
< 3 months after MI, SCA
< 12 months after DES
> 12 months in high-risk stents[2]
Low-risk cardiac situations
High-risk intracranial neurosurgery
All surgery
Elective surgery
Vital/urgent surgery[3]
High-risk surgery
Delay surgery
Excessive bleeding risk[4]
Stop clopidogrel Maintain aspirin
Stop 5 days before operation as needed
Operation under continuous treatment
Stop clopidogrel + bridging
Maintain aspirin
Restart clopidogrel 24 h postop
Eberli D, et al, J Urol (2010) 183: 2128
1 HR patients = documented CV disease, DM, multiple risk factors
2 HR stents = multiple / long / proximal / bifurcation stents, previous stent thrombosis

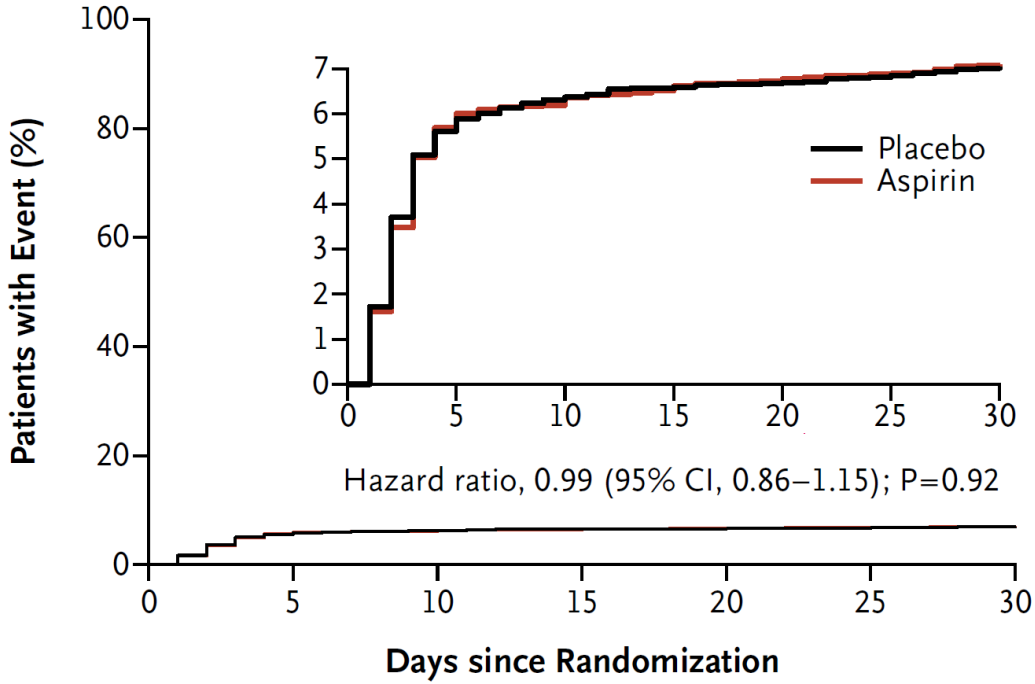
Conclusion

- Patients under DAPT need this treatment
- The duration of DAPT is limited
- Do not plan operations during the time of DAPT
- Operations that cannot be postponed after DAPT
  - ➔ Always avoid within first 6 months
  - ➔ Do not stop aspirin (except the day of operation)
  - ➔ Use the bridging concept
    - – Clopidogrel: Stop 5 days prior to the operation
    - – Prasugrel: Stop 7 days prior to the operation
    - – Ticagrelor: Stop 5 days prior to the operation
    - – Start GPIIb/IIIa antagonist 3 days prior to the operation
  - ➔ Restart aspirin and the second platelet inhibitor on POD 1 without loading dose

Aspirin in Patients Undergoing Noncardiac Surgery

- **PRT, 2 x 2 factorial design (Aspirin +/-, Clonidin +/-)**
- **10'010 patients**
  - ➔ **Initiation stratum (n=5'628) without prior Aspirin**
  - ➔ **Continuation stratum (n=4'382) with prior Aspirin**
- **1-Outcome: Composite of death and MI**
- **Exclusion criteria**
  - ➔ **DES < 1 year**
  - ➔ **BMS < 6 weeks**
  - ➔ **Few patients with stents outside these time intervals included**

Devereaux P. J. et al., New Engl J Med (2014) 370: 1494
Supplementary Appendix



Safety outcomes				
Life-threatening bleeding	87 (1.7)	73 (1.5)	1.19 (0.88–1.63)	0.26
Major bleeding	230 (4.6)	188 (3.8)	1.23 (1.01–1.49)	0.04
Clinically important hypotension	2143 (42.9)	2096 (41.8)	1.03 (0.97–1.09)	0.37
Stroke	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

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Supplemental Table 3: Effects of Aspirin on the 30-day outcomes in the Continuation Stratum

Outcome	Aspirin (N=2191)	Placebo (N=2191)	Hazard Ratio (95% CI)	P Value
Primary outcome – no. (%)				
mortality or nonfatal myocardial infarction	169 (7.7)	170 (7.8)	1.00 (0.81-1.23)	0.97
Secondary outcomes – no. (%)				
mortality, nonfatal myocardial infarction, or nonfatal stroke	177 (8.1)	175 (8.0)	1.01 (0.82-1.25)	0.90
second composite outcome*	196 (9.0)	193 (8.8)	1.02 (0.83-1.24)	0.86
Tertiary outcomes – no. (%)				
total mortality	27 (1.2)	24 (1.1)	1.12 (0.65-1.95)	0.67
vascular mortality	16 (0.7)	16 (0.7)	1.00 (0.50-2.00)	1.00
myocardial infarction	151 (6.9)	153 (7.0)	0.99 (0.79-1.24)	0.93
nonfatal cardiac arrest	5 (0.2)	4 (0.2)	1.25 (0.34-4.66)	0.74
cardiac revascularization	10 (0.5)	10 (0.5)	1.00 (0.42-2.40)	1.00
pulmonary embolism	18 (0.8)	12 (0.6)	1.50 (0.72-3.12)	0.27
deep venous thrombosis	10 (0.5)	14 (0.6)	0.71 (0.32-1.61)	0.41
new clinically important atrial fibrillation	58 (2.7)	41 (1.9)	1.42 (0.95-2.11)	0.09
peripheral arterial thrombosis	8 (0.4)	7 (0.3)	1.14 (0.41-3.15)	0.80
amputation	5 (0.2)	5 (0.2)	1.00 (0.29-3.45)	1.00
re-hospitalization for vascular reasons	32 (1.5)	19 (0.9)	1.69 (0.96-2.98)	0.07
acute kidney injury with receipt of dialysis†	19 (0.9)	8 (0.4)	2.41 (1.05-5.51)	0.04
Safety outcomes – no. (%)				
life-threatening bleeding	38 (1.7)	26 (1.2)	1.46 (0.89-2.41)	0.13
major bleeding	100 (4.6)	90 (4.1)	1.11 (0.84-1.48)	0.47
clinically important hypotension	936 (42.7)	921 (42.0)	1.02 (0.93-1.11)	0.72
stroke	13 (0.6)	7 (0.3)	1.86 (0.74-4.66)	0.19
congestive heart failure	23 (1.1)	17 (0.8)	1.35 (0.72-2.54)	0.34
infection	197 (9.0)	206 (9.4)	0.96 (0.79-1.16)	0.66
sepsis	99 (4.5)	102 (4.7)	0.97 (0.74-1.28)	0.83

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Supplementary Appendix

Association Between Postoperative Troponin Levels and 30-Day Mortality Among Patients Undergoing Noncardiac Surgery

- **Prospective cohort study in 15’133 patients**
- **Outcome**
  - ➔ **Postoperative troponin POD 0 - 3**
  - ➔ **Correlation of postoperative troponin and 30 day mortality**

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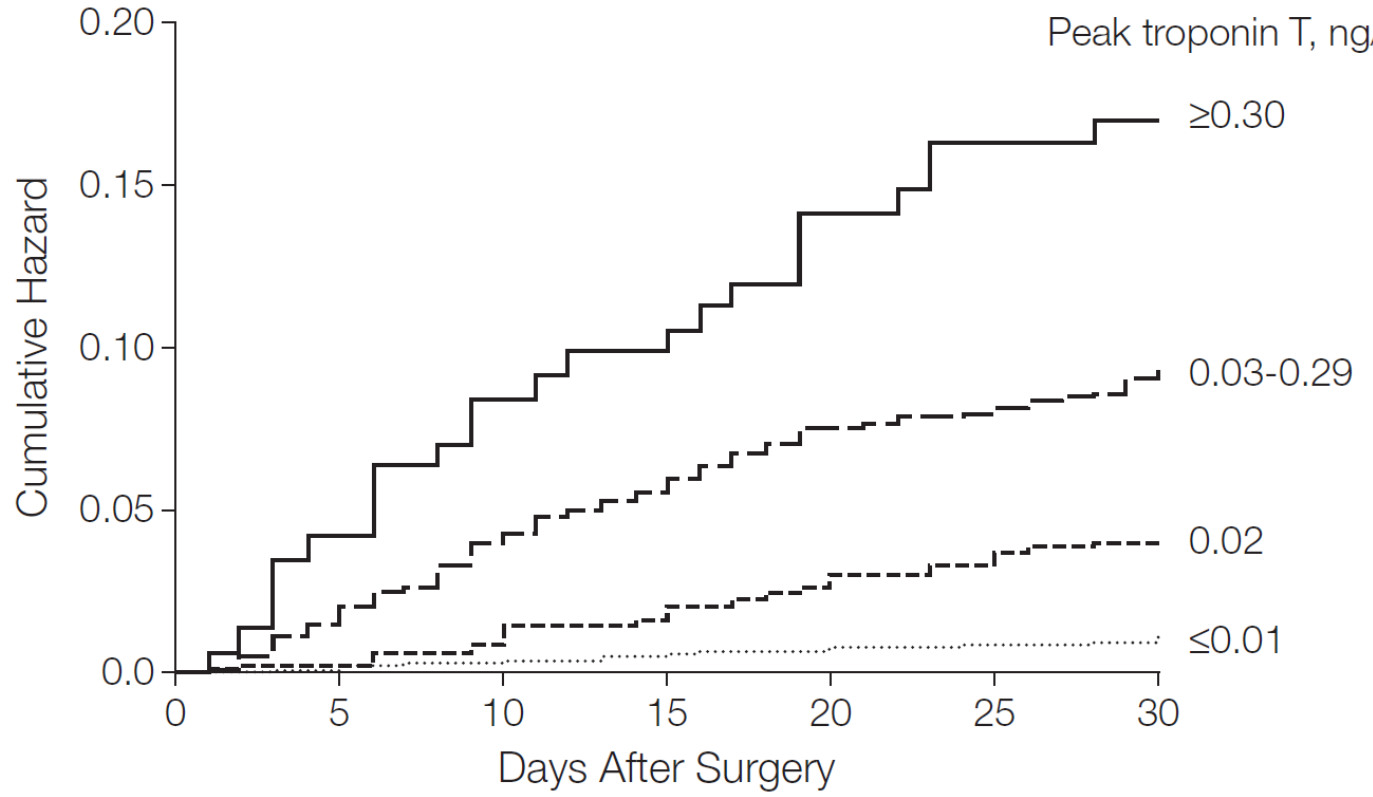
Figure 2. Kaplan-Meier Estimates of 30-Day Mortality Based on Peak Troponin T Va



No. at risk

Peak troponin T, ng/mL							
≥0.30	142	136	129	127	121	118	117
0.03-0.29	1121	1103	1075	1058	1036	1030	1018
0.02	494	492	489	485	480	477	473
≤0.01	13376	13348	13300	13271	13250	13230	13209

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Table 6 Pharmacological features of non-vitamin K antagonist oral anticoagulants

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Target	IIa (thrombin)	Xa	Xa	Xa
Application	Oral	Oral	Oral	Oral
Hours to C^{max}	1.25–3	2–4	3–4	1–2
Pro-drug	Yes	No	No	No
Food interactions	No	No	No	No
Bioavailability (%)	6.5	80–100	50	62
Drug interactions	P gp inhibitors or inductors	CYP3a4 inhibitors or inductors P gp inhibitors or inductors	CYP3a4 inhibitors or inductors P gp inhibitors or inductors	P gp inhibitors
Median half-life (hours)	12–14	7-11 (11–13 in the elderly)	12	6-11
Renal clearance (%)	85	33	27	37-50
Dose regimen	b.i.d.	q.d.	b.i.d.	q.d

b.i.d. = *bis in diem* (twice daily); C_{max} = maximum concentration; CYP3a4 = cytochrome P3a4 enzyme; P gP = platelet glycoprotein; q.d. = *quaque die* (once daily).

Normally no bridging

Normal bleeding risk: Stop NOAC 2-3 t1/2 (Rivaroxaban: > 36 h)

Increased bleeding risk: Stop NOAC 4-5 t1/2 (Rivaroxaban: > 60 h)

Postoperative restart: Delay of 1-2 (3-5) days

Treatment: Vague: PCC, aPCC, hemodialysis for dabigatran

Kristensen S.D. et al., Eur Heart J (2014) 35: 2383