CONTROVERSES ET ACTUALITÉS EN CHIRURGIE VASCULAIRE
CONTROVERSIES & UPDATES IN VASCULAR SURGERY
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Should We Stop Clopidogrel Before Open Vascular Surgery?

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Disclosure

I have **no financial relationships** to disclose.

Je n'ai **aucune relation financière** à déclarer.

Critical Issue

Management of perioperative clopidogrel

- Increasing number of patients on clopidogrel, in combination with ASA, for longer periods
- Expanding indications: DES, generic drug…
- Concerns about safety: predictor of reoperation for bleeding → exposure ≤ 5d of CABG

→ Variations in vascular practice

Purpose of the Study

Design: Prospective non-randomized comparative

Aim: impact of preop exposure to clopidogrel & ASA on bleeding complications

Inclusion criteria:

All consecutive patients (2005-mid 12) undergoing

1. Carotid Endarterectomy (CEA)
2. Abdominal Aortic Bypass (AAB)
3. Lower Extremity Bypass (LEB)

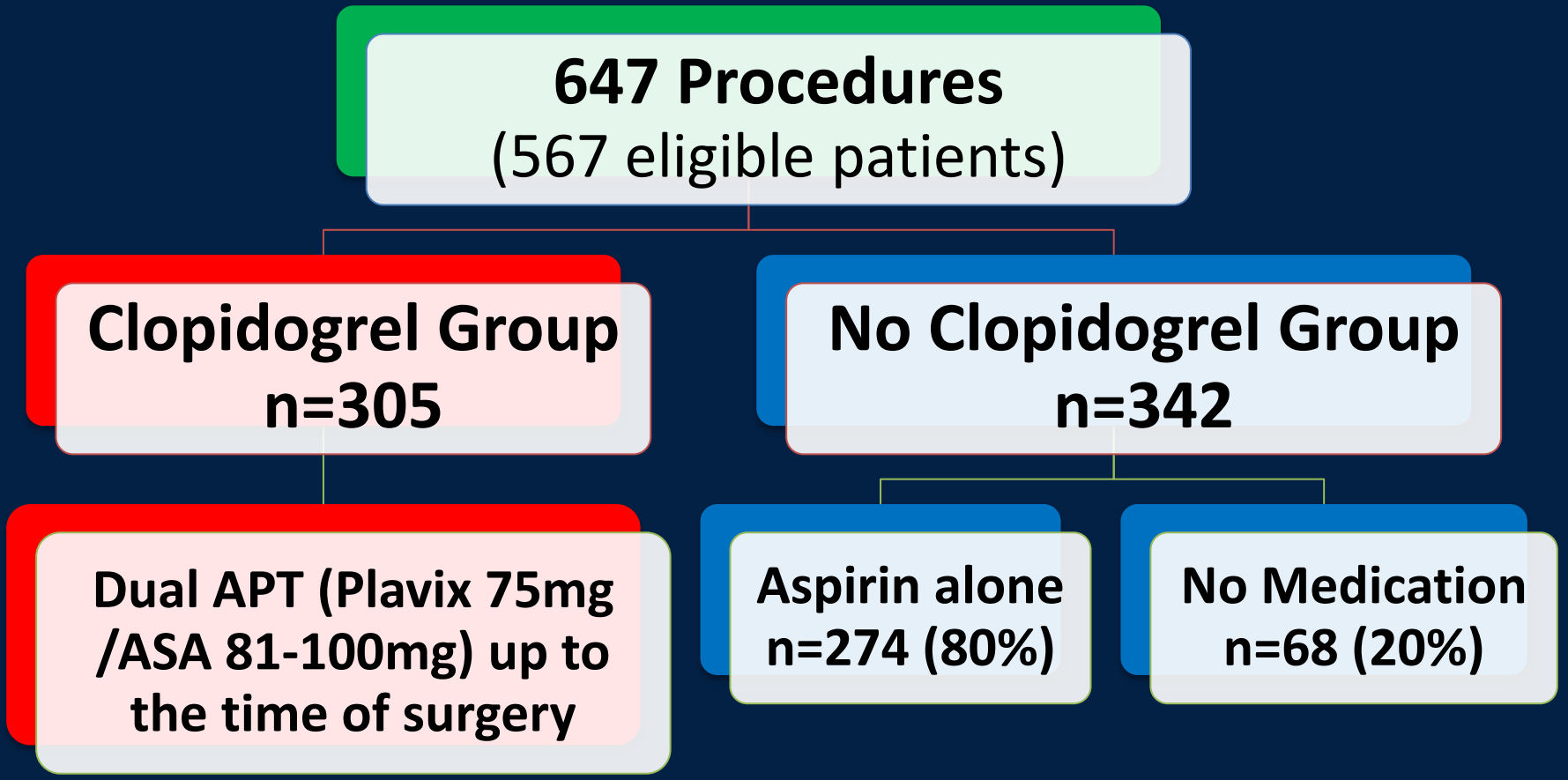
Approved by the institutional Ethics Committees

Exclusion Criteria

- Emergency surgery for hemorrhage (RAAA & trauma)
- Endovascular aneurysm repair (EVAR)
- Congenit./acquired bleeding disorder (Hemophilia...)
- Simultaneous CEA and CABG
- Preoperative blood transfusions (anemia)

***Informed consent**, explaining potential risks of surgery under clopidogrel, not given*

Patient Population



Study End Points

Primary composite end point

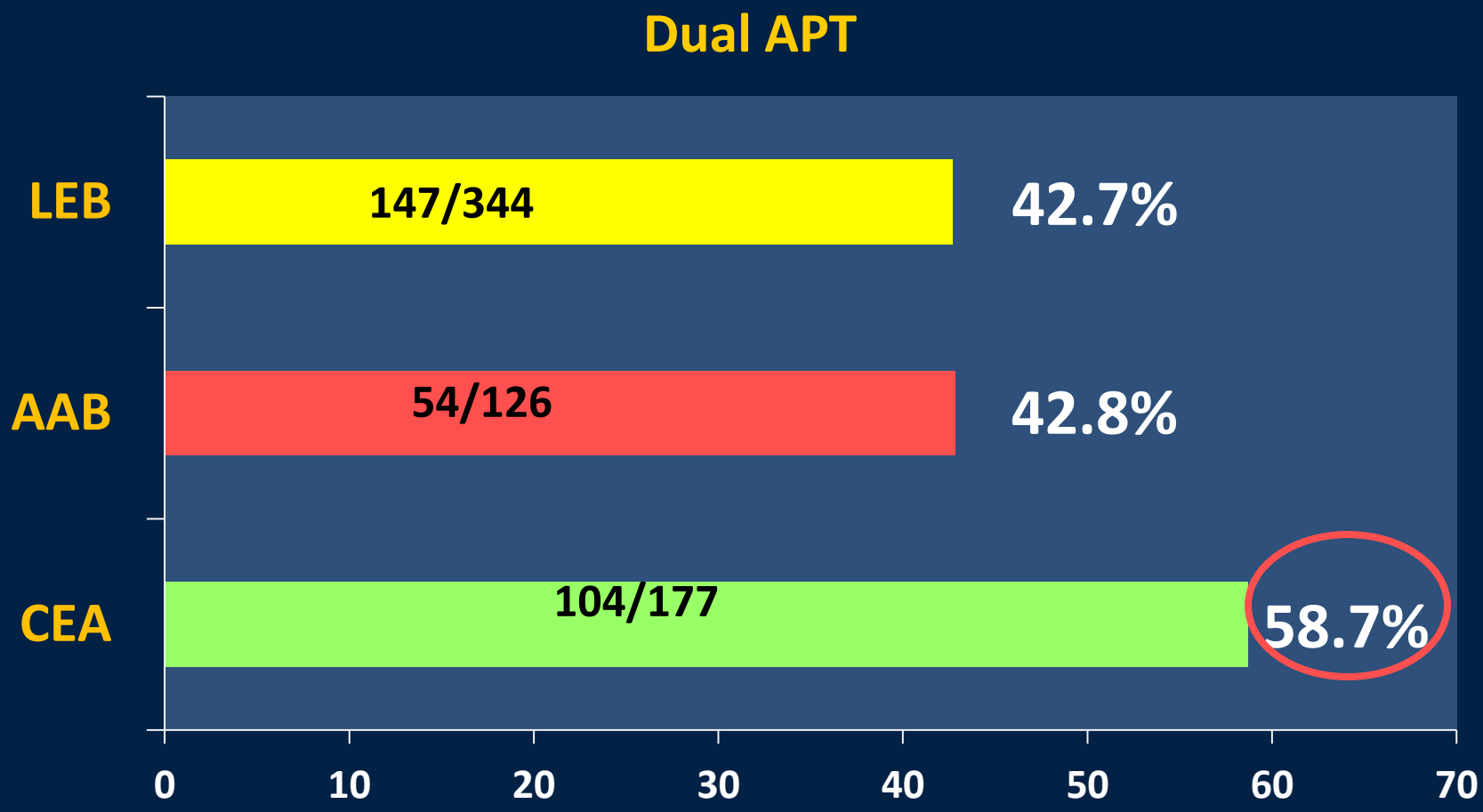
- Reoperation for bleeding & bleeding-related death

Secondary end points

- Blood transfusion requirements
- Hematoma formation
- Duration of procedures
- Hospital & ICU length of stay (LOS)

RESULTS

Clopidogrel use (47%) reflects today's "real world" practice



Patient Demographics & Comorbidities (%)

	Clopidogrel	No Clopidogrel	*P value*
Procedures, total	**305**	**342**	
Patients, (Male %)	269 (73)	298 (76)	NS
Mean age, y (+/- SD)	69	68	NS
Hypertension	**269 (88.1)**	**274 (80)**	**.036**
Smoking (current)	195 (63.9)	215 (62.8)	NS
Dyslipidemia	**241 (79)**	**219 (64)**	**.001**
Diabetes mellitus	**173 (56.7)**	**145 (42.3)**	**.003**
PCI / Stenting	**143 (46.8)**	**27 (7.9)**	**<.001**
Drug-eluting stent	**39 (27)**	**0**	**<.001**
CABG	44 (14.4)	55 (16)	NS
Prior LE bypass	**33 (11)**	**7 (2)**	**.002**
Peripheral Stenting	**30 (9.8)**	**11 (3.2)**	**.008**
Statins	**226 (74)**	**163 (47.6)**	**<.001**

Primary End Point

Similar results

	Clopidogrel n=305	No clopidogrel n=342	*P*
Composite endpoint	2 (0.65)	1 (0.3)	NS
Mortality	0	0	NS
Re-exploration rate	2 (0.65)	1 (0.3)	NS
Bleeding source	Tissue oozing	Wound	

Dual APT vs. ASA Alone	Clopidogrel n=305	ASA n=274	*P*
Primary EP	2 (0.65)	1 (0.36)	NS

Endpoints Classified by Type of Procedure(%)

AAB n=126

	Clopido n=54	No Clo n=72	*P*
Primary End Point	0	0	NS
MACE	1 (1.8)	1 (1.4)	NS
Transfusion requirements			
Incidence	39 (72)	50 (69)	NS
Mean units of PRBC	1.6 ±0.7	1.6 ±0.6	NS
Hematoma	0	0	NS
Operative time, min	122 ±28	123 ±28	NS
ICU stay, days	1.1 ±0.8	1.3 ±0.6	.021
Hospital stay, d	6.3 ±1.6	6.2 ±1.8	NS

Ecchymotic suffusions #hematomas

Endpoints Classified by Type of Procedure(%)

LEB n=344

	Clopidogrel	No clopidogrel	*P*
	n=147	n=197	
Primary End Point	1 (0.68)	1(0.5)	NS
Transfusion requirements			
Incidence	22 (15)	22 (11)	NS
Mean units of PRBC	1.5 ±0.6	1.3 ±0.8	.04
Hematoma	3 (2)	2 (1)	NS
Infrapopliteal Bypass	27 (18.4)	19 (9.6)	.003
Operative time, min	88 ±33	79 ±27	NS
Hospital stay, d	4.7 ±1.9	4.5 ±2.3	NS

Endpoints Classified by Type of Procedure(%)

CEA n=177

	Clopidogrel	No clopidogrel	*P*
	n=104	n=73	
Symptomatic stenosis	63 (61)	26 (36)	.015
Primary End Point	1 (0.96)	0	NS
Stroke / Death	0	0	NS
Hematoma	1(1)	0	NS
Operative time, min	69 ±11	65 ±9	NS
Hospital LOS, d	2.8 ±0.8	2.7 ±0.6	NS

ICU stay 12-24h for all patiens

Variability of Clopidogrel Responsiveness

Impact of platelet function on results?

P2Y12 receptor VASP test on 40 clopidogrel patients

5 pts excluded for drug interactions w/ omeprazol & CCBs

Outcomes not different

	Good responders n=27 (77%)	Low responders n=8 (23%)	*P*
Primary EP	**0**	**0**	**NS**
Hematoma	**1 (3.7)**	**0**	**NS**

→ Requires further investigations

Few Studies in Vascular Surgery: Conflicting Results

Author	Year	AP Therapy	Outcome
Fleming	2009	19 clopidogrel-treated vs.81 untreated pts (CEA)	**No difference in bleeding complications**
Wait	2010	42 pts on clopidogrel up to 5 days pre-CEA	**Significant increase in nonop. neck swelling**
Rosen-baum	2010	50 pts on clopidogrel vs. 171 pts on ASA (CEA)	**Significantly more hematomas requiring re-exploration (16 v 1.7%)**
Stone	2011	7-y review of NE Registry from 66 surgeons:n=1246 clopidogrel within 48h	**Not associated w/ major bleeding across spectrum of operations, incl. EVAR**

Study Limitations

1- Not a randomized controlled trial

- Recent ACS or DES pts at high CV risk, if withheld
  → RCT only in selected patients
- Opportunity for bias ↓ (protocol/analyst)

2- Same surgical team

- Multicentred (university & community hospitals)
- Validation by other surgeons

Conclusions

1. Discontinuation of preoperative clopidogrel with aspirin is unnecessary in peripheral arterial surgery
2. Bleeding risks are minimized with growing familiarity & meticulous hemostasis