SHORT DAPT VS. LONGER DAPT: WHOM AND How? CLINICIAN AND TRIALIST'S PERSPECTIVE

Robert W. Yeh, MD MSc MBA Director, Richard A. and Susan F. Smith Center for Outcomes Research in Cardiology Associate Chief, Interventional Cardiology, Beth Israel Deaconess Medical Center Associate Professor of Medicine, Harvard Medical School

#TCTAP2021





th Israel Deaconess edical Center



HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Funding and Disclosures

Industry Funding and Disclosures

Abbott Vascular: Scientific Advisory Board, CTO Proctoring, Consulting, Investigator-initiated research grant Astra Zeneca: Consulting, Investigator-initiated research grants

Boston Scientific: Scientific Advisory Board, CTO Proctoring, Consulting, Investigator-initiated research grants

Medtronic: Scientific Advisory Board, Consulting, Investigator-initiated research grants

SAFE-PAD Study – (Co-PI) is jointly sponsored by Bard, Boston Scientific, Cook, Phillips, and Medtronic.

Non-Industry Funding

National Heart, Lung and Blood Institute R01HL136708 (EXTEND Study) K23HL118138 (DAPT Score) K24HL150321



Current Guidelines Support Individualizing DAPT Duration

Individualized treatment ("selective") is favored over one-size-fits all ("routine")

Antiplatelet therapy after stenting	2		
DAPT is indicated for at least 1 month after BMS implantation.	<u> </u>	A	791,799-801
DAPT is indicated for 6 months after DES implantation.	1	8	799,802,803
Shorter DAPT duration (<6 months) may be considered after DES implantation in patients at high bleeding risk.	lib	A.	804,805
Life-long single antiplatelet therapy, usually ASA, is recommended.	1	A	776,794
Instruction of patients about the importance of complying with antiplatelet therapy is recommended.	1	c	
DAPT may be used for more than 6 months in patients at high ischaemic risk and low bleeding risk.	lib	c	



In patients with ACS treated with coronary stent implantation who have tolerated DAPT without bleeding complication and who are not at high bleeding risk (e.g., prior bleeding on DAPT, coagulopathy, oral anticoagulant use) continuation of DAPT for longer than 12 months may be reasonable (16,22-26,28,30,40,41,43,53,54,72).



Medical Center

In patients with ACS treated with DAPT after DES implantation who develop a high risk of bleeding (e.g., treatment with oral anticoagulant therapy), are at high risk of severe bleeding complication (e.g., major intracranial surgery), or develop significant overt bleeding, discontinuation of $P2Y_{12}$ therapy after 6 months may be reasonable (17-21,34,36,37).



Beth Israel Deaconess HARVARD MEDICAL SC

How We Identify Patients for Short vs. Long Strategies?

Clinical Factors

Anatomical Factors

Procedural Factors



r HARVARD MEDICAL

<u>Clinical Factors</u> – High Bleeding Risk

In 2018, ARC (developed the ST definition) developed a definition of HBR patients

- Includes PCI candidates who have a postprocedure 1-year >4% risk of a major bleed (BARC 3-5) and/or a >1% risk of intracranial bleeding
- HBR status is considered present for patients who meet at least 1 major or 2 minor HBR criteria

Major criterion

Minor criterion



Urban, P, et al. European Heart Journal (2019) 40, 2632–2653.

Validated Bleeding Scores

PARIS Bleeding Score

- Developed in an allcomers registry
- Validated in ADAPT-DES (C-stat 0.64)
- Factors include
 - Older age Extremes of BMI Smoking Anemia Triple therapy

Baber, Mehran et al.

6 Babe Beth Israel Deaconess Beth Israel Deaconess Commence Harvard Medical School

PRECISE-DAPT Bleeding Score

- Developed in pooled cohort of 8 RCTs
- Validated in PLATO Trial and Bern PCI registry (c-stat 0.66-0.70)
- Factors include

Lower hemoglobin Higher WBC count

- Older Age
- Lower Cr clearance
- Prior bleeding
- Costa, Valgimigli et al.

Shorter vs. Longer DAPT Based on Bleeding Risk vs. Lesion Complexity

CENTRAL ILLUSTRATION: PRECISE-DAPT Score and Complex Percutaneous **Coronary Intervention**



Short DAPT: 3-6 mo Longer DAPT: 12-24 mo

Costa, F. et al. J Am Coll Cardiol. 2019;73(7):741-54.



Medical Center

7

Beth Israel Deaconess

What About Low Bleeding Risk Patients?

CENTRAL ILLUSTRATION: PRECISE-DAPT Score and Complex Percutaneous **Coronary Intervention**



75% of patients had PRECISE-DAPT < 25 and would have benefited from LONGER DAPT duration. with clear signal of greater benefit for more complex disease.

Costa, F. et al. J Am Coll Cardiol. 2019;73(7):741-54.



Medical Center

Beth Israel Deaconess HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

ACS patients, particularly those with high DAPT Score, benefit most from long DAPT

Variable	Points			DADT	0	0 1 0			00	DAD	T 0			
Patient Characteristic		L L	Q		Score	e -2 to U)		Q3	= DAP		re 2		
Age		A	Qź	2 = DAPI	Score	e 1			Q4	= DAP	I Sco	re > 2	2	
≥ 75	-2	S S	4.0%	S	tent		Ν	Луос	ardia		GUS	том	oder	ate/
65 - <75	-1	lth	3.0%	Thro	ombosi	S		Infar	ction		Sev	vere B	leed	ing
< 65	0	nor	3.070	Q1 Q	2 Q3	Q4	Q1	Q2	Q3	Q4	Q1 1.97	% Q2	Q3	Q4
Diabetes Mellitus	1	12 r	2.0% -									1.179	6	
Current Cigarette Smoker	1	ν. VS.	1.0% -										0.69	%
Prior PCI or Prior MI	1	30	0.0% -	1				—	—	—		_		0.03%
CHF or LVEF < 30%	2	e e	1.0% -	-0.07% -0.06	5%		_0 73%	-0.59%						
Index Procedure Characteristic		renc	2.0% -		-1.34%		-0.7370							
MI at Presentation	1	ffe	,.		-	2.18%								
Vein Graft PCI	2	- <u> </u>	-3.0% -					-	2.56%					
Stent Diameter < 3mm	1	∖isk	4.0%						-	3.48%				

Yeh, Secemsky, Kereiakes et al. JAMA. 2016.

Going too short in ACS

SMART-DATE: 6 vs. 12+ months DAPT after ACS (2700 pts). SAPT regimen = ASA monotherapy



Hahn et al. Lancet 2018.



Anatomical Factors: Coronary Complexity

Pooled analysis of 6 RCTs Comparing 3 to 6 months DAPT Vs. \geq 12 months DAPT

Complex Features: 3 vessels treated ≥ 3 stents placed ≥ 3 lesions treated Bifurcation with 2 stents Total stent length > 60 mm CTO Effect of ≥12 Months Versus 3 or 6 Months DAPT on the Risk of Major Adverse Cardiac Events According to Procedural Complexity





Lesion Complexity and Outcomes of Extended Dual Antiplatelet Therapy After Percutaneous Coronary Intervention



My takeaway:

Coronary complexity should influence DAPT duration most within 1st year of PCI esp among lower bleeding risk patients.

Thereafter, it likely matters much less, and is superceded by other clinical risk factors

Medical Center

How Should We Give Shorter vs. Longer DAPT?

Short DAPT – Bleeding risk exceeds ischemic

- Do we give DAPT for 1 month? 3 months?
- Discontinue the P2Y12 inhibitor at the end or discontinue ASA?
- Which P2Y12 inhibitor do we use?

Longer DAPT - Ischemic risk exceeds bleeding

- Do we give DAPT for 12 months? 24 months? 30 months? Indefinite?
- Discontinue the P2Y12 inhibitor at the end or discontinue ASA? Lower the dose of P2Y12?
- Which P2Y12 inhibitor do we use?



Meta-Analysis Randomized short DAPT trials included

Trial	Blind	Intervention	Control	Follow-up
GLOBAL-LEADERS	Open label	Ticagrelor monotherapy after month 1	Clopidogrel (stable CAD) or ticagrelor (ACS) + ASA 75- 100mg daily	12 months
SMART CHOICE	Open label	Any P2Y ₁₂ i monotherapy after month 3	Any $P_2Y_{12}i + ASA 81-200mg$ daily after month 1	12 months
STOPDAPT 2	Open label	Clopidogrel monotherapy after month 1	Clopidogrel + ASA 75- 100mg daily	12 months
TWILIGHT	Double blind	Ticagrelor monotherapy after month 3	Ticagrelor + ASA 81-100mg daily	15 month (randomized at month 3)
TICO	Open label	Ticagrelor monotherapy after month 3	Ticagrelor + ASA 100mg daily	12 months

O'Donoghue ML, et al. Circulation. 19 Jun 2020, online ahead of print. DOI: 10.1161/CIRCULATIONAHA.120.046251.

Meta-Analysis Clinical outcomes



O'Donoghue ML, et al. Circulation. 19 Jun 2020, online ahead of print. DOI: 10.1161/CIRCULATIONAHA.120.046251.

Conclusions

- The cliché holds true: there is no one size fits all for DAPT strategies.
- Shortening duration in stable PCI likely does not meaningfully increase ischemic events, nor decrease bleeding events in low risk patients
- Use tools to identify HBR patients most likely to benefit from short duration
- Remember that many patients are not HBR, and will still benefit from longer durations of DAPT, particularly ACS patients and high DAPT score.
- Within these broad recommendations, there are still many different approaches clinicians might take.





Beth Israel Deaconess Medical Center

Richard A. and Susan F. Smith Center for Outcomes Research in Cardiology

Thank you!

E: ryeh@bidmc.harvard.edu



