

Non distal Left Main- BMS or DES? Does it really matter?

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Facts

- Previously, unprotected left main [UPLM] disease has almost exclusively resulted in utilizing a surgical revascularization treatment strategy.

Facts

- Only modest evidence has been available to support the indication for UPLM percutaneous revascularization in patients ineligible for bypass surgery; with even less evidence to endorse PCI as an otherwise routine therapy in this indication.

WHY SO?

Early Experiences of POBA in UPLM

- O'Keefe *et al* [[Am J Cardiol. 1989;64:144-147](#)], reported a 6 month mortality rate of around 55% in 26 patients with UPLM disease [elastic recoil, no stents].

BMS in UPLM

- As early as 1992 [[Macaya *et al*, Am J Cardiol. 1992;70:105-107](#)].
- Multicenter registry of UPLM in the mid-90's [[Ellis S *et al*, Circulation. 1997;96:3867-3872](#)] reported:
 - For patients with acute myocardial infarction, technical success was achieved in 75%, and survival to hospital discharge was 31%.

BMS in UPLM

- For elective patients, technical success was achieved in 98.9%, and in-hospital survival was strongly correlated with left ventricular ejection fraction ($P = .003$) [Ellis S *et al*, *Circulation*. 1997;96:3867-3872].

BMS in UPLM

- Longer-term event (death, infarction, or bypass surgery) -free survival was correlated with ejection fraction ($P < .001$) and was inversely related to presentation with progressive or rest angina ($P < .001$) [Ellis S *et al*, *Circulation*. 1997;96:3867-3872].

BMS in UPLM

- Surgical candidates with ejection fractions $\geq 40\%$ had an in-hospital survival of 98% and a 9-month event-free survival of $86 \pm 5\%$.
- Patients with ejection fractions $< 40\%$ had 67% and $22 \pm 12\%$ in-hospital and 9-month event-free survivals, respectively [[Ellis S *et al*, Circulation. 1997;96:3867-3872](#)].

Facts

- Accordingly, intersociety guidelines have recommended:
 - Against UPLM percutaneous revascularization as an optional therapy in individuals eligible for CABG (Class III).
 - Supported the indication with a still uncertain benefit (Class IIb) only in circumstances of excessive surgical risk.

Facts

- Recent improvements in PCI techniques, in parallel with the benefits of drug-eluting stents (DES) to reduce clinical restenosis, have enabled further investigation in catheterization-based treatment strategies as possible alternative therapeutic options.

Enthusiasm for DES in UPLM: Road to SYNTAX

- Following their introduction to the market in 2003; DES performance in left main PCI has been evaluated in nonrandomized, observational surveys with abbreviated longitudinal follow-up.

Enthusiasm for DES in UPLM: Road to SYNTAX

- Compared with conventional BMS, DES revascularization in UPLM disease was associated with clinically meaningful reductions in angiographic restenosis and the need for repeat revascularization.

Non-Randomized Studies of BMS vs. DES in UPLM Disease

Non-Randomized Studies

- A number of non-randomized trials compared BMS to DES (consecutive patients, from the pre-DES era followed by the DES era).
- In all but one study, the percentage of distal/bifurcation UPLM disease was significantly higher in the DES group.

	BMS/DES	TVR	MACE	Distal LM
Park <i>et al</i> (2005)	121/102	17%/2%	26% BMS 8% DES	43% BMS 71% DES
Chieffo <i>et al</i> (2005)	64/85	31%/19%	35.9%/20%	58% BMS 81% DES
Valgimigli <i>et al</i> (2005)	86/95	12%/6%	14%/45%	15%BMS 40% DES
Wood <i>et al</i> . (2005)	100/61	N/A	46%/13%	N/A
Carrie <i>et al</i> (2006)	57/49	18%/2%	35.1%/4%	100% in BOTH GROUPS

	BMS/DES	TVR	MACE	Distal LM
Sheiban <i>et al</i> (2006)	69/72	24.3%/13.6%	45%/17%	70% BMS 58% DES
Christiansen <i>et al</i> (2006)	58/46	N/A	21%/19%	N/A
Han <i>et al</i> (2006)	34/176	14.7%/6.8%	26.5%/11.4%	32.1% BMS 72.1% DES
Gao <i>et al</i> (2008)	224/220	11.6%/5.9%	16.5%/9.5%	32.1% BMS 75.5% DES
Palmerini <i>et al</i> (2008)	1111/342	16.1%/11.8%	N/A	57.6% BMS 70% DES

ONE Randomized Study of BMS vs.
DES in UPLM Disease

	BMS/ DES	Restenosis Rate	TVR	MACE	Distal LM
Englis <i>et al</i> (2007)	50/50	11%/6%	16%/2%	30%/13%	68% BMS 81% DES

What Do These Studies Tell Us?

- TVR/TLR advantage of DES over BMS in UPLM Intervention.
- Different series of landmark analyses of cardiac mortality consistently showed that the advantage of DESs over BMSs obtained in the vulnerable period of restenosis was maintained up to 2 years

What Do These Studies Tell Us?

- One study demonstrated:
 - Restenosis was a potential mechanism leading to mortality in patients with ULMCA stenosis treated using PCI.
 - Prevention of restenosis was associated with improved survival.

What Do These Studies Tell Us?

MORTALITY BENEFIT OF DES over BMS in UPLM
IS RELATED TO NOTABLE REDUCTIONS IN
RESTENOSIS & TVR/TLR RATES

The Achilles' Heel of Percutaneous Treatment

- Valgimigli et al [[J Am Coll Cardiol 2006;47:1530–1537](#)]. identified distal lesion location as an independent predictor of poor outcome following UPLM PCI.
- The cumulative incidence of target vessel revascularization was 13% and 3% for distal and proximal lesions, respectively.

DES versus CABG in UPLM Interventions-The Evidence

Road to SYNTAX: **MAIN COMPARE**

- Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty versus Surgical Revascularization involving 2,240 patients with UPLM disease.
- Non Randomized Trial: compared outcomes according to treatment with percutaneous revascularization (DES 71%/BMS 29%) or CABG

Road to SYNTAX: **MAIN COMPARE**

- Patients followed for approximately 3 years.
- Treatment with DES was associated with a significantly lower rate of freedom from repeat revascularization versus CABG (90.7% vs. 98.4%, p 0.001). Caution: Non-Randomized.

Seung KB, Park DW, Kim YH, et al. Stents versus coronary-artery bypass grafting for left main coronary artery disease. *N Engl J Med* 2008;358:1781–92.

Road to SYNTAX: **MAIN COMPARE**

- Importantly, no significant differences in safety end points including freedom from death (DES 91.0% vs. CABG 93.1%, $p=0.26$) or the composite end point of death, myocardial infarction, or stroke were identified.

Seung KB, Park DW, Kim YH, et al. Stents versus coronary-artery bypass grafting for left main coronary artery disease. *N Engl J Med* 2008;358:1781–92.

SYNTAX Trial

- **SYNERGY** Between Percutaneous Coronary Intervention With **TAXUS** and Cardiac Surgery trial comparing CABG with PCI for left main/multi-vessel disease.

SYNTAX Trial

- Patient treatment assignment was stratified according to the presence of significant UPLM disease, representing a patient cohort (n 705) with approximately 60% bifurcation disease and 13% isolated left main disease (i.e., no additional target lesions).

SYNTAX Trial

- There were NO DIFFERENCES in 1-year individual outcomes of death or myocardial infarction, despite significantly higher rates of stroke in the CABG group (2.7% CABG vs. 0.3% PCI, $p=0.009$).

SYNTAX Trial

- Repeat revascularization was more common with PCI (6.7% CABG vs. 12.0% PCI, $p=0.02$) and was particularly driven by higher rates among patients with left main disease treated for **additional 2-vessel** (15.3% vs. 7.7%, $p=0.08$) **or 3-vessel** (14.8% vs. 6.0%, $p=0.02$) disease.

What Do These Studies Tell Us?

- Bifurcation is commonly characterized by higher risk of restenosis than other lesion subsets.
- TLR/TVR benefit of surgery over DES related to the higher percentage of Distal UPLM disease [Obviously CABG would not be affected by UPLM lesion location].

What Do These Studies Tell Us?

- NO SIGNIFICANT DIFFERENCES in survival
[Possibly because restenosis with DES is more focal, thus not affecting survival].

BMS vs. DES in Non-Bifurcation
UPLM PCI

	BMS/DES	TVR	MACE	Distal LM
Tamburino <i>et al</i> (2009)	145/334	10.7%/7.9% (P=0.6)	37.8%/25% (P=0.06, 0.01, 0.047)	0%

BMS vs. DES in Non-Bifurcation UPLM PCI

- Non-randomized study.
- BMS group presented a higher risk profile.
- Three contemporary methods of adjustments (using covariate, propensity score as covariate or propensity score matching) were performed in order to account for possible confounders.

BMS vs. DES in Non-Bifurcation UPLM PCI

- Investigators observed a trend for a reduction of mortality with DES vs. BMS, with a magnitude ranging from 58–69% for death from cardiac causes ($P = 0.06$, $P = 0.01$ and $P = 0.047$ for cardiac mortality).
- Absence of a real advantage of DES in reducing TLR ($p=0.6$).

Disparity Between Survival & TLR Benefit?

- A. Learning curve in favor of DES.
- B. Closer/stricter angiographic follow-up with DES.
- C. Prolonged double antiplatelet therapy [survival benefit, no effect on restenosis].

The Question

Is the well-documented effectiveness of DES vs. BMS in reducing the need for TLR in patients who undergo PCI for treatment of CAD questionable when the issue of non-bifurcation UPLM disease is addressed?

Answer

YES, it is questionable.

No concrete answers [No randomized trials].