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Coronary artery bypass grafting for left main disease and the risk of stroke: Incidence, aetiology and prevention

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ABSTRACT

This review explores the association between left main disease and the increased risk of perioperative stroke following coronary artery bypass grafting, specifically addressing the potential underlying mechanisms and its potential prevention. In particular, this correlation appears stronger for patients with left main disease when compared to patients with isolated triple vessel disease. Even though evidence on this topic is limited and of modest quality, there appears to be a significant association between ascending aorta atherosclerosis and coronary artery disease. Furthermore, there seems to be a relationship between the severity and extent of carotid artery stenosis and coronary artery disease. Carotid artery disease is itself associated with atherosclerosis of the ascending aorta, a well-recognised risk factor for postoperative atheroembolic stroke. The association between left main disease, ascending aorta atherosclerosis and carotid artery stenosis may reflect an increased systemic atherosclerotic burden and hence explain, at least partially, the higher risk of perioperative cerebrovascular events. Potential pre-, intra- and post-operative strategies for stroke prevention are discussed.

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Introduction

Coronary artery bypass grafting (CABG) has been the standard of care for patients with complex coronary artery disease due to its long-term safety and efficacy, which are superior to percutaneous coronary intervention (PCI) even in the era of drug-eluting stents.^{1–5} However, CABG is associated with a higher risk of perioperative stroke than PCI. Despite the progressive decline in perioperative stroke rate

over time,⁶ the incidence remains 2.1%–5.2%^{7,8} and the mortality 0%–38%.⁹

The landmark Synergy between PCI Taxus and Cardiac Surgery (SYNTAX) trial suggested that the higher stroke risk for CABG over PCI was restricted to patients with left main disease (LMD)^{10,11} and the difference persisted at 5-years of follow-up (Table 1).^{12–14} This apparently increased risk of stroke associated with LMD in comparison with 3VD was supported in the recent meta-analysis,¹⁵ which reported that at all time intervals of follow-up the hazard ratio for

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Table 1 – Comparison of stroke risk for patients with left main disease and three-vessel disease at 5-year and 10-year follow-up.

Study	3VD			LMD		
	PCI (% stroke)	CABG (% stroke)	PCI vs CABG (OR [95% CI])	PCI (% stroke)	CABG (% stroke)	PCI vs CABG (OR [95% CI])
PRECOMBAT trial ⁶⁴	NA	NA	NA	0.7	0.7	0.99 [0.14–7.02]
LE MANS trial ⁶⁵				4.3	6.3	2.85 [0.40–20.4]
SYNTAX trial ^{14,12}	2.7	3.4	0.85 [0.43–1.71]	1.5	4.3	0.33 [0.12–0.92]
Athappan et al. ¹⁵	3.8	4.6	0.82 [0.72–0.95]	1.7	4.7	0.53 [0.36–0.77]

3VD, three-vessel disease; CABG, coronary artery bypass grafting; CI, confidence interval; LMD, left main disease; OR, odds ratio; PCI, percutaneous coronary intervention.

perioperative stroke was consistently lower for patients with LMD than 3VD (Table 2).

This review explores the potential underlying mechanisms for the increased risk of perioperative cerebrovascular events in patients with LMD when compared to patients with 3VD as well as recommended preventative strategies.

Methods

Medline 1980 to May 2015 was used from the PubMed interface. The primary search terms used were “Coronary Artery Disease”[Mesh] AND (“Carotid Artery Diseases”[Mesh] OR “Aortic Disease”[Mesh]). Citations were screened at the title and abstract level and retrieved as full reports if they were clinical studies and mentioned directly or indirectly a relationship between carotid, aortic and coronary disease. The full texts of all potential articles were reviewed in detail and only studies that separated patients with LMD and 3VD were included. The bibliography of retained studies was used to seek additional relevant studies.

This search strategy resulted in 773 papers of which 14 papers were considered eligible based on the abstract and/or full-text. A further 4 papers were identified on reference lists of other papers. Therefore, a total of 18 papers were included in the final analysis (Table 3 in Supplementary material).

LMD and aortic disease

Isolated LMD is often due to ostial stenosis (about 30% in the SYNTAX trial), which may be more representative of atherosclerosis of the ascending aorta and thus carry an increased risk of atheroembolism,^{16–18} particularly in the presence of extensive aortic disease.¹⁹ The higher stroke risk associated with atherosclerosis of the proximal aorta may also be related to the common co-existence with disease of the carotid and/or other intracranial arteries²⁰ as well as clinical risk factors for postoperative stroke, including age and impaired left ventricular ejection fraction,¹⁸ which may serve as surrogate markers for aortic atheroma.

LMD and carotid artery disease

The association between LMD and carotid artery disease as well as its impact on perioperative cerebrovascular events have mainly been indirectly addressed in studies with other primary objectives^{21–30} (Table 3 in Supplementary material).

Most evidence hitherto available supports a direct correlation between the severity of carotid artery disease and the extent of coronary artery disease and this association appears to be stronger for LMD than 3VD irrespectively of carotid artery disease severity,^{27–29,31} with the former carrying a two-fold higher risk of severe carotid artery disease.³²

Table 2 – Early, delayed and late stroke risk for patients with multivessel and left main disease (adapted from Athappan 2014¹⁵).

Time period	Studies	Patients	PCI (% stroke)	CABG (% stroke)	PCI vs CABG (OR [95% CI])		
					Overall	3VD	LMD
Within 30 days	35	39,447	0.3	1.4	0.26 [0.20–0.35]	NA	NA
1 year	35	39,447	1.2	2.2	0.55 (0.42–0.71)	0.55 [0.41–0.74]	0.47 [0.28–0.78]
2 years	22	29,389	3.0	3.7	0.78 (0.66–0.92)	0.77 [0.62–0.95]	0.60 [0.40–0.89]
3 years	17	40,584	6.6	9.2	0.79 (0.67–0.92)	0.77 [0.70–0.86]	0.56 [0.36–0.77]
4 years	9	21,960	3.5	4.3	0.74 (0.56–0.97)	0.72 [0.60–0.86]	0.36 [0.19–0.69]
5 years	13	22,518	3.5	4.4	0.79 (0.69–0.91)	0.82 [0.72–0.95]	0.53 [0.36–0.77]

The risk of early and delayed stroke (within 48 h and 30 days of intervention, respectively) was significantly higher for CABG when compared to PCI. On the contrary, the risk of late stroke appeared to be evenly distributed between the 2 strategies during follow-up, thus suggesting that a late catch-up phenomenon of stroke in the PCI arm is unlikely.

3VD, three-vessel disease; CABG, coronary artery bypass grafting; CI, confidence interval; LMD, left main disease; OR, odds ratio; PCI, percutaneous coronary intervention.

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