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Date:
2018-09-01

Citation:
Theuerle, J., Yudi, M. B., Farouque, O., Andrianopoulos, N., Scott, P., Ajani, A. E., Brennan, A., Duffy, S. J., Reid, C. M. & Clark, D. J. (2018). Utility of the ACC/AHA lesion classification as a predictor of procedural, 30-day and 12-month outcomes in the contemporary percutaneous coronary intervention era. Catheterization and Cardiovascular Interventions, 92 (3), pp.E227-E234. https://doi.org/10.1002/ccd.27411.

Utility of the ACC/AHA Lesion Classification As a Predictor of Procedural, 30-day and 12-month Outcomes in the Contemporary Percutaneous Coronary Intervention Era

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Keywords: Lesion complexity, PCI, clinical outcomes
Word Count: 3,199 words.
Running Head: Utility of ACC/AHA lesion classification in contemporary PCI

ABSTRACT

Background:

Correlations between the ACC/AHA coronary lesion classification and clinical outcomes in the contemporary percutaneous coronary intervention (PCI) era are not well established.

Methods:

We analyzed clinical characteristics and outcomes according to ACC/AHA lesion classification (A, B1, B2, C) in 13,701 consecutive patients from the Melbourne Interventional Group (MIG) registry. Patients presenting with STEMI, cardiogenic shock and out-of-hospital cardiac arrest were excluded. The primary endpoints were 30-day and 12-month mortality. Secondary endpoints were procedural success as well as 30-day and 12-month major adverse cardiac events.

Results:

Of the 13,701 patients treated, 1,246 (9.1%) had type A lesions, 5,519 (40.3%) had type B1 lesions, 4,449 (32.5%) had Type B2 lesions and 2,487 (18.2%) had Type C lesions. Patients with type C lesions were more likely to be older and have impaired renal function, diabetes, previous myocardial infarction, peripheral vascular disease and prior bypass graft surgery (all $p<0.01$). They were also more likely to require rotational atherectomy, drug-eluting stents and longer stent lengths (all $p<0.01$). Increasing lesion complexity was associated with lower procedural success (99.6% vs. 99.1% vs. 96.6% vs. 82.7%, $p<0.001$) and worse 30-day (0.2% vs. 0.3% vs. 0.7% vs. 0.6%, $p<0.001$) and 12-month mortality (2.2% vs. 2.0 % vs. 3.2% vs. 2.9%, $p <0.01$). Kaplan Meier analysis showed complex lesions (type B2 and C) had lower survival at 12-months ($p=0.003$).

Conclusions:

PCI to more complex lesions continues to be associated with lower procedural success rates as well as inferior medium-term clinical outcomes. Thus the ACC/AHA lesion classification should still be calculated pre-procedure to predict acute PCI success and clinical outcomes.

INTRODUCTION

In 1988, the American College of Cardiology and the American Heart Association (ACC/AHA) developed a lesion morphology classification scheme to identify patients most suitable for percutaneous coronary intervention (PCI) with the highest likelihood of procedural success [1, 2]. Consequently, it also identified those at high risk for acute complications.

Historically, lesions are classified across a 3-tier system (A, B and C) based on 11 morphological characteristics. An early modification dividing the intermediate category into B1 and B2 at present time widely accepted [3]. Currently, a binary classification is often employed with A or B1 lesions denoted as "simple", and B2 or C lesions being "complex".

This classification is well validated in percutaneous coronary angioplasty (PTCA) [3], directional atherectomy [4] and rotational atherectomy [5]. In addition, higher lesion complexity using the simplified binary cut-offs has been linked with a poorer prognostic outcome following bare-metal stent deployment [6] and in PCI for acute coronary syndromes [7]. However, these results were challenged by a number of later studies that reported no significant difference in complication rate amongst type A, B and C lesions [8-10]. Furthermore, in a contemporary PCI context Khattab and colleagues showed no prognostic difference between simple and complex lesions in the medium term for patients who received coronary revascularization with sirolimus-eluting stents [11].

Given the conflicting nature of the contemporary data available, the aim of this study was to assess the suitability of the ACC/AHA coronary lesion criteria as a predictor of procedural success, in-hospital complications as well as 30-day and 12-month clinical outcomes in the modern PCI era.

METHODS

A cohort of 13,701 consecutive patients undergoing PCI between 2005 and 2013 were included in our study. A total of 16,249 lesions were treated. All were registered with the Melbourne Interventional Group (MIG), a collaborative consortium of interventional cardiologists practising across 6 major tertiary hospitals in Victoria, Australia [12, 13]. Case reports forms detailing demographic, clinical, procedural and in-hospital outcome data are prospectively collected using standardized definitions and post-procedural outcomes are assessed at 30 days and 12 months.

The MIG registry is coordinated by the Centre of Cardiovascular Research and Education in Therapeutics; an independent research body within the School of Public Health and Preventive Medicine at Monash University (Melbourne, Australia). An audit of a number of verifiable fields from 5% of randomly selected procedures at each institution is undertaken periodically [14]. In the most recent audit, 27 fields were assessed with data accuracy of 98%. This compares favourably to audits from other large registries [15]. The ethics committee in each participating hospital has approved the MIG registry, including the use of "opt-out" consent. This means that consent is presumed unless the patient "opts out". All participating sites give each patient a "Patient Information Sheet". If a patient informs a staff member that they do not wish to participate, the patient's data are not collected.

Patients were stratified according to the ACC/AHA classification criteria as either A, B1, B2 or C (Table 1) [3, 16]. At the time of PCI, a qualified interventional cardiologist classified the lesion being treated. Lesions graded as either A or B1 were considered simple, while those assessed as B2 or C were complex.

Patients presenting with either ST-elevated mycocardial infarction (STEMI), cardiogenic shock or out-of-hospital cardiac arrest were excluded from this study.

The primary endpoints were 30-day and 12-month mortality. Secondary endpoints were acute procedural success and in-hospital complications as well as 30-day and 12-month major adverse cardiac events (MACE). MACE was defined as a combination of mortality, myocardial infarction, and target vessel revascularization. Acute complications included coronary dissection or perforation, in-hospital death, peri-procedural myocardial infarction (MI), cardiac tamponade, cardiogenic shock,

stroke, bleeding, emergency PCI, and unplanned coronary artery bypass grafting (CABG). Procedural success was defined as: <50% residual stenosis for angioplasty or <20% residual stenosis for a stented lesion. Bleeding was defined as a drop of haemoglobin >3.0gm/dl and/or blood transfusion requirement and/or prolonged hospital stay due to bleeding. A stroke is defined by a persistent loss of neurological function (lasting at least 24 hours) caused by an ischaemic or haemorrhagic event, confirmed by CT scan. Clinical criteria for cardiogenic shock were: hypotension (a systolic blood pressure of ≤90 mmHg for at least 30 minutes or the need for supportive measures to maintain a systolic blood pressure of ≥90 mmHg); end-organ hypoperfusion (cool extremities or a urine output ≤30ml/h and a heart rate ≥60 beats per minute); or cardiac index of ≤2.2 L/min per square meter of body-surface area and a pulmonary capillary wedge pressure ≥15 mmHg. Emergency PCI was defined as an unplanned PCI during hospitalization and prior to discharge, which occured as a complication of the index PCI, such as stent thrombosis or dissection with target vessel occlusion.

Statistical analyses were performed using Stata 13.1 (StataCorp LP, College Station, TX, USA). Continuous variables are expressed as mean ± standard deviation (SD), and categorical data are expressed as numbers/percentages. Continuous variables were compared using the Kruskal-Wallis equality-of-populations rank test. Categorical variables were compared using Fisher's exact or Pearson's chi-square tests as appropriate. P values less than 0.05 were considered statistically significant. Cumulative incidence of mortality was estimated by the Kaplan-Meier method and the log-rank test was used to evaluate differences between groups. Cox proportional hazard modelling was used to identify univariate and multivariate predictors of 30-day and 12-month mortality. Univariate variables with a p-value ≤0.10 were tested for evidence of collinearity using pairwise Pearson's correlation coefficient and Variance Inflation Factor. If evidence was found, what we considered the more clinically relevant variable was selected. All remaining variables were then included in a backward selection process to determine the relevant multivariate models. The variables used were: lesion classification, age, sex, eGFR, smoking history, hypertension, diabetes, hypercholesterolaemia, family history of coronary disease, previous MI, previous PCI, previous CABG, heart failure, peripheral vascular disease, cerebrovascular disease, left

ventricular ejection fraction, multivessel CAD, angina type, chronic lung disease, obstructive sleep apnea, rheumatoid arthritis, glycoprotein IIb/IIIa use, drug-eluting stent use, long stent (>20mm), small diameter (<2.5mm), treated lesion location (ostial, bifurcation, left main, LAD, circumflex, right coronary artery, bypass graft) and chronic total occlusion.

RESULTS

Baseline Characteristics

13,701 patients were enrolled in the study with 16,249 lesions undergoing PCI. There were 1,335 (8.2%) with type A lesions, 6,290 (38.7%) with type B1, 5,491 (33.8%) with type B2 and 3,133 (19.3%) with type C. Demographic and baseline clinical characteristics are tabulated in Table 2. The cohort was predominantly male (74.6%) with a mean age of 65.2±11.6 years. There was a graded increase in the percentage of patients with diabetes, previous MI, previous PCI/CABG, peripheral vascular disease, cerebrovascular disease, renal impairment (eGFR<30ml/min/1.73m^2), reduced left ventricular ejection fraction (<30%) and multi-vessel CAD with increasing lesion complexity (all $p < 0.01$).

Procedural Characteristics

Table 3 outlines procedural and lesion characteristics. Patients with increasingly complex lesions were more likely to undergo left main PCI, IVUS guidance and rotational atherectomy (all $p < 0.001$). Furthermore, the more complex lesions required larger calibre guiding catheters, longer stent lengths and received a much higher proportion of drug-eluting stents. Chronic total occlusions made up 23.5% of type C lesions, respectively.

In-Hospital Complications and Clinical Outcomes

In-hospital complications and outcomes are outlined in Table 4. There was an inverse relationship between lesion complexity and procedural success. Furthermore, as lesion complexity increased there was a significant increase in peri-procedural complications including coronary dissection and perforation, peri-procedural myocardial infarction, no re-flow, cardiogenic shock and unplanned CABG (all p value for trend <0.01). There was no significant difference between lesion classes with regards to urgent PCI, stroke, in-hospital major bleeding and mortality.

Mortality at 30 days was highest in those with complex lesions (A 0.2%, B1 0.3%, B2 0.7% and C 0.6%; $p < 0.01$; Table 5) and this trend was maintained at 12 months (A 2.2%, B1 2.0%, B2 3.2% and C 2.9%; $p < 0.01$; Table 5). MI, TVR and MACE were also progressively higher with increasing lesion complexity at both 30 days and 12 months (Tables 5).

Kaplan Meier survival curve shows a significantly worse 12-month survival in patients with complex lesions (p = 0.003, Figure 1). Multivariate predictors of 30-day and 12-month mortality are shown in Figure 2A and 2B respectively.

DISCUSSION

Three important conclusions can be drawn from this study regarding the modified ACC/AHA lesion morphology classification scheme and its application in the contemporary PCI era. Firstly, ACC/AHA classification remains a strong predictor of procedural success and there were higher rates of unsuccessful PCI with increasingly complex lesions. Secondly, more complex lesions were associated with higher rates of multiple in-hospital complications, including coronary artery dissection, vessel perforation, myocardial infarction, cardiogenic shock and unplanned CABG. Lastly, higher lesion complexity correlated with higher mortality rates and major adverse cardiovascular events at both 30-days and 12-months.

In the coronary angioplasty era, Ellis and colleagues [3] demonstrated markedly lower success rates and increasing complications with higher degrees of lesion complexity. In comparison, the much higher procedural success rates seen in our study (A lesion: 99.6% vs. 92%, B1 lesion: 99.1% vs. 84%; B2 lesion: 96.6% vs. 76%; C lesion: 82.7 vs. 61%) highlights the improvement in PCI techniques and performance over the past three decades. What has remained constant is the stepwise decrease in success rates across the lesion classification categories. Similarly, while overall complication rates have decreased, they are still proportional to lesion complexity. This has implications for informed consent of patients prior to PCI. Zaacks and colleagues [8] found that specific lesion characteristics, namely total occlusions and tortuosity, rather than ACC/AHA lesion classification to be predictive of complications but this study was limited by small sample size. We included tenfold more patients and this greater power has allowed us to discriminate across the four lesion classification categories, in spite of the low numbers of unsuccessful procedures and complications in contemporary PCI. Our data therefore reinforces the utility of lesion classification at time of PCI to assess success rate and complication risk.

Modern PCI techniques, improved equipment and the availability of optimal pharmacotherapy have been postulated as reasons for the diminished predictive ability of lesion classification [8-11]. Utilization of these advances in interventional cardiology was evident in our cohort of patients, particularly in those with complex lesions as they were more likely to be treated with rotational atherectomy, drug-eluting stents and glycoprotein IIb/IIIa inhibitors, along with higher rates of IVUS-guided PCI. While the

greater use of these newer technologies were associated with significant improvement in procedural outcomes in our study, they do not completely eliminate the risk posed by more complex lesions. It is also worth considering that the advancement in technology may also increase the complexity of lesions having attempted PCI, such as chronic total occlusion.

Kastrati and colleagues found the short- and medium-term prognostic value of the ACC/AHA lesion classification was preserved in PCI in an observational study with bare-metal stents [6]. However, Khattab *et al.* did not find a significant difference in death, myocardial infarction and target vessel revascularisation between simple and complex lesions following PCI with 1st generation sirolimus-eluting stents, although a trend towards increased myocardial infarction and death in complex lesion patients was identified [11]. In comparison with these studies, the main advantage of our study is its larger population and the use of the complete ACC/AHA classification rather than the dichotomy of simple vs. complex lesion. Furthermore, our study is a more robust representation of contemporary PCI as we included consecutive patients irrespective of initial procedural success whereas the German Cypher Registry used in Khattab *et al* [11] only included patients where a sirolimus-eluting stent was successfully deployed. Although a successfully treated complex lesion may have similar clinical outcomes to a simple lesion, it does not diminish the prognostic value of the lesion classification to predict procedural success. Indeed, our study strengthens the contention that the ACC/AHA lesion classification translates beyond procedural success and also predicts medium term-clinical outcomes.

It is plausible that lesion complexity may be a marker of more advanced atherosclerosis. We have shown that patients with increasingly more complex lesions are more likely to have a history of previous MI, PCI, CABG and higher rates of both multi-vessel coronary artery disease and peripheral vascular disease. They also have a higher burden of co-morbidities, namely diabetes mellitus, chronic renal impairment and left ventricular dysfunction. This is consistent with previous studies [3, 6, 11]. While these co-morbidities may partially explain the worse outcomes with more complex lesions, the fact remains that lesion class is closely linked to short- and medium term MACE in contemporary PCI and lesion classification remains a predictor, albeit modest, of 30-day mortality.

Our study has several limitations that warrant discussion. First and most importantly, inter-operator variability exists in assessing coronary lesion morphology according to the ACC/AHA classification system and independent external assessment of coronary angiograms was not performed. Variation by one classification has been observed in over 30% of cases in a previous study, however variation by two classifications (eg. B1 lesion classified as a C lesion) is rare [3]. Secondly, given the retrospective nature of our study there may be unaccounted factors that influence procedural decision-making and outcomes. Thus our results are hypothesis generating rather than conclusive. Thirdly, we do not capture details of interventional methods thus we cannot account for advancements in chronic total occlusion and bifurcation techniques as well as the availability of newer equipment.

CONCLUSION

The present study confirms that the ACC/AHA lesion morphology classification remains an important predictor of procedural success, in-hospital complications and medium term-outcomes. Thus it should still be an important part of risk-benefit assessment and informed consent of patients prior to PCI.

Figure 1. Kaplan-Meier Survival Curves

Figure 2. Independent Predictors of 30 Day and 12 Month Mortality

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Acknowledgements:

The Melbourne Interventional Group acknowledges unrestricted educational grant funding from: Abbott Vascular, Astra-Zeneca, Medtronic, MSD, Pfizer, Servier, and The Medicines Company. These companies do not have access to the data, and do not have the right to review manuscripts before publication.

Dr. Yudi is supported by a combined National Health and Medical Research Council Postgraduate Scholarship (APP 1115163) and a National Heart Foundation Health Professional Scholarship (Award ID 101130). Dr. Duffy's & Professor Reid's work is funded by National Health and Medical Research Council of Australia Grants.

The Melbourne Interventional Group acknowledges and thanks all patients who have been involved in the registry.

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Table 1 – Angiographic Characteristics of Type A, B and C Lesions[3]

Type A Lesions	
Discrete (<10 mm length)	Little or no calcification
Concentric	Less than totally occlusive
Readily accessible	Not ostial in location
Non-angulated segment, <45°	No major branch involvement
Smooth Contour	Absence of thrombus
Type B Lesions **B1: one adverse characteristic; B2: ≥2 adverse characteristics**	
Tubular (10 – 20 mm length)	Moderate to heavy calcification
Eccentric	Total occlusion <3 months old
Moderate tortuosity of proximal segment	Ostial in location
Moderately angulated segment, >45° and <90°	Bifurcation lesions requiring double guide wires
Irregular contour	Some thrombus present
Type C Lesions	
Diffuse (>2 cm length)	Total occlusion >3 months old
Excessive tortuosity of proximal segment	Inability to protect major side branches
Extremely angulated segments, >90°	Degenerated vein grafts with friable lesions

Table 2 – Patient Demographic and Baseline Clinical Characteristics

	A (N=1,246)	B1 (N=5,519)	B2 (N=4,449)	C (N=2,487)	P- value
Age, years (mean±SD)	64.8±11.8	64.8±11.4	65.5±11.7	65.7±11.6	<0.01
Male gender	892 (71.6)	4,143 (75.1)	3,341 (75.1)	1,908 (76.7)	0.01
BMI (kg/m^2)	28.4±5.1	28.8±5.3	28.6±5.3	28.5±5.3	0.06
Hypertension	905 (72.7)	4,021 (72.9)	3,149 (70.8)	1,876 (75.5)	<0.01
Hypercholesterolaemia	971 (78.1)	4,320 (78.4)	3,405 (76.6)	1,988 (80.1)	<0.01
Diabetes Mellitus	315 (25.3)	1,492 (27.0)	1,245 (28.0)	795 (32.0)	<0.01
Current smoker	245 (19.7)	1,111 (20.2)	861 (19.4)	420 (16.9)	0.28
Family History of CAD	503 (40.8)	2,185 (39.9)	1,755 (40.0)	938 (38.2)	0.36
Previous MI	388 (31.2)	1,777 (32.2)	1,408 (31.7)	1,032 (41.5)	<0.01
Previous PCI	370 (29.7)	1,692 (30.7)	1,348 (30.3)	849 (34.1)	<0.01
Previous CABG	94 (7.5)	511 (9.3)	530 (11.9)	420 (16.9)	<0.01
Prior Heart Failure	52 (4.2)	238 (4.3)	190 (4.3)	162 (6.5)	<0.01
Peripheral Vascular Disease	63 (5.1)	392 (7.1)	356 (8.0)	249 (10.0)	<0.01

Chronic Lung Disease	**120 (9.7)**	**571 (10.4)**	**514 (11.6)**	**273 (11.0)**	**0.13**
eGFR > 60 ml/min/1.73m2	**964 (78.4)**	**4,218 (77.7)**	**3,384 (77.2)**	**1,825 (74.4)**	**<0.01**
eGFR 30-59 ml/min/1.73m2	**243 (19.8)**	**1,053 (19.4)**	**870 (19.8)**	**520 (21.2)**	**<0.01**
eGFR <30 ml/min/1.73m2	**22 (1.8)**	**157 (2.9)**	**132 (3.0)**	**107 (4.4)**	**<0.01**
Ejection Fraction >45%	**809 (81.0)**	**3,869 (82.8)**	**3,079 (81.0)**	**1,618 (77.3)**	**<0.01**
Ejection Fraction 30-45%	**167 (16.7)**	**738 (15.8)**	**658 (17.3)**	**416 (19.9)**	**<0.01**
Ejection Fraction <30%	**23 (2.3)**	**67 (1.4)**	**64 (1.7)**	**59 (2.9)**	**<0.01**
Stable Angina	**660 (53.0)**	**2,722 (49.4)**	**1,892 (42.6)**	**1,305 (52.5)**	**<0.01**
Unstable Angina	**166 (13.3)**	**832 (15.1)**	**578 (13.0)**	**328 (13.2)**	**<0.01**
NSTEMI	**419 (33.7)**	**1,960 (35.6)**	**1,975 (44.4)**	**852 (34.3)**	**<0.01**

Data are presented as mean ± SD or number(percentage). BMI = body mass index. CAD = coronary artery disease. MI = myocardial infarction. PCI = percutaneous coronary intervention. CABG = coronary artery bypass graft surgery. eGFR = estimated glomular filtration rate. NSTEMI = non-ST elevation myocardial infarction.

Table 3 – Procedural Characteristics According to Lesion Complexity.

	A (N=1,246)	B1 (N=5,519)	B2 (N=4,449)	C (N=2,487)	P- value
Femoral Access	1,119 (89.8)	4,929 (89.3)	3,873 (87.1)	2,195 (88.3)	<0.01
≥7F Catheter Used	64 (3.9)	535 (7.9)	731 (14.1)	434 (10.9)	<0.01
Multivessel CAD	669 (54.1)	3,242 (59.1)	2,783 (62.8)	1,704 (68.8)	<0.01
Rotational Atherectomy	1 (0.1)	32 (0.5)	68 (1.3)	110 (4.1)	<0.01
Glycoprotein IIb/IIIa Use	120 (9.7)	686 (12.4)	915 (20.6)	469 (18.9)	<0.01
Drug-eluting stent	492 (30.5)	2,522 (45.7)	2,465 (55.4)	1,505 (60.5)	<0.01
Bare-metal stent	725 (58.2)	2,835 (51.4)	1,779 (40.0)	564 (22.7)	<0.01
Balloon angioplasty only	29 (2.3)	162 (2.9)	205 (4.6)	418 (16.8)	<0.01
Total Stent Length (mm)	14.2±5.3	16.6±5.6	19.5±8.0	27.4±12.6	<0.01
Bifurcation	27 (1.7)	458 (6.8)	944 (18.2)	334 (12.4)	<0.01
Ostial lesion	38 (2.3)	352 (5.2)	562 (10.8)	196 (7.3)	<0.01
Left main PCI	20 (5.2)	105 (6.0)	118 (7.6)	102 (10.2)	<0.01
Proximal LAD PCI	202 (12.4)	1,003 (14.9)	790 (15.2)	364 (13.5)	0.014
Bifurcation lesion	27 (1.7)	458 (6.8)	944 (18.2)	334 (12.4)	<0.01
SVG-PCI	30 (1.9)	137 (2.0)	160 (3.1)	185 (6.9)	<0.01
IVUS-guided PCI	14 (0.9)	64 (1.0)	79 (1.5)	47 (1.8)	<0.01

Data are presented as mean ± SD or number(percentage). CAD = coronary artery disease. MI = myocardial infarction. PCI = percutaneous coronary intervention. SVG = saphenous vein graft. IVUS = intravascular ultrasound.

Table 4 – In-hospital Outcomes and Complications

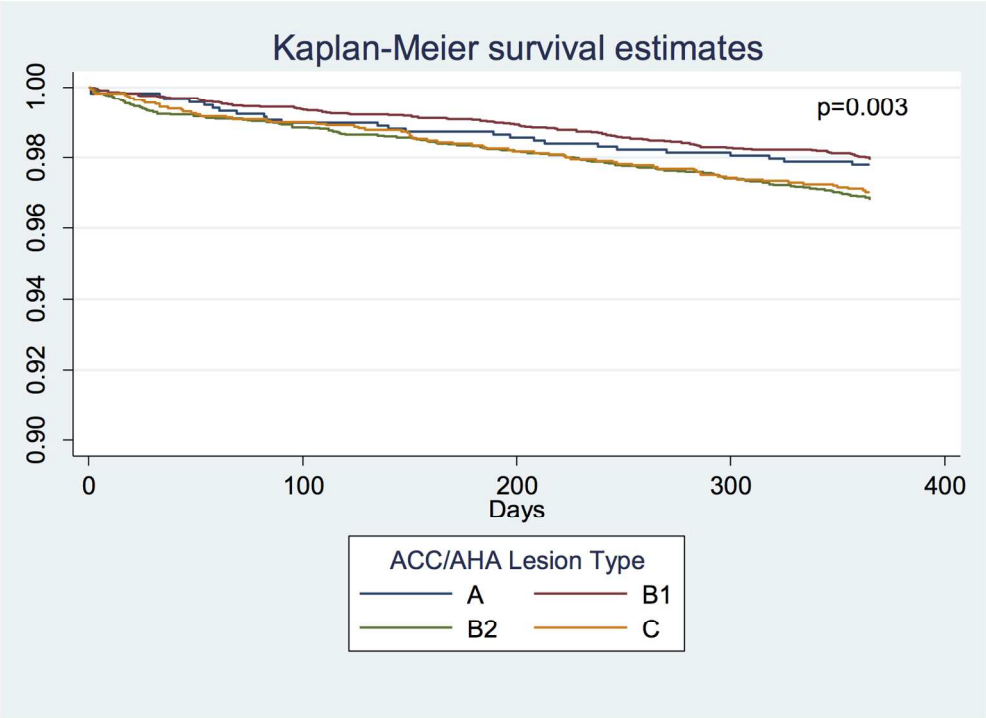
	A (N=1,246)	B1 (N=5,519)	B2 (N=4,449)	C (N=2,487)	P- value
Procedural Success	1,240 (99.6)	5,462 (99.1)	4,290 (96.6)	2,056 (82.7)	<0.01
Coronary dissection	38 (2.3)	233 (3.5)	307 (5.9)	220 (8.2)	<0.01
Coronary perforation	1 (0.06)	10 (0.2)	8 (0.1)	25 (0.9)	<0.01
No Reflow	25 (1.7)	89 (1.5)	153 (3.2)	99 (3.9)	<0.01
Peri-procedural MI	10 (0.8)	29 (0.5)	59 (1.3)	47 (1.9)	<0.01
Emergency PCI	4 (0.3)	16 (0.3)	16 (0.4)	9 (0.2)	0.84
Unplanned CABG	1 (0.1)	6 (0.1)	29 (0.7)	46 (1.9)	<0.01
Tamponade	0	0	1 (0.02)	3 (0.2)	0.02
Cardiogenic Shock	1 (0.1)	5 (0.1)	11 (0.3)	14 (0.6)	<0.01
Stroke	3 (0.2)	5 (0.1)	4 (0.1)	5 (0.2)	0.32
Major bleeding	22 (1.8)	77 (1.4)	68 (1.5)	41 (1.7)	0.72

Data are presented as number(percentage). MACE = major adverse cardiovascular event. MI = myocardial infarction. PCI = percutaneous coronary intervention. CABG = coronary artery bypass graft surgery.

Table 5 – Clinical Outcomes at 30 Days and 12-Months

	A (N=1,246)	B1 (N=5,519)	B2 (N=4,449)	C (N=2,487)	P- value
In-hospital Death	3 (0.2)	8 (0.1)	12 (0.3)	9 (0.4)	0.28
In-hospital MACE	17 (1.4)	53 (1.0)	97 (2.2)	87 (3.5)	<0.01
30-day mortality	3 (0.2)	15 (0.3)	31 (0.7)	14 (0.6)	<0.01
30-day MI	16 (1.3)	71 (1.3)	94 (2.1)	76 (3.1)	<0.01
30-day TVR	10 (0.8)	45 (0.8)	81 (1.8)	103 (4.1)	<0.01
30-day MACE	26 (2.1)	112 (2.0)	167 (3.8)	156 (6.3)	<0.01
30-day CVA	5 (0.4)	9 (0.2)	12 (0.3)	8 (0.3)	0.33
30-day readmission	106 (8.6)	563 (10.2)	462 (10.4)	319 (12.9)	<0.01
12-month Mortality	26 (2.2)	105 (2.0)	131 (3.2)	68 (2.9)	<0.01
12-month MI	45 (3.8)	223 (4.3)	232 (5.6)	144 (6.2)	<0.01
12-month TVR	61 (5.1)	295 (5.7)	310 (7.5)	251 (10.9)	<0.01
12-month MACE	109 (9.2)	511 (9.9)	531 (12.9)	380 (16.5)	<0.01
12-month CVA	10 (0.8)	32 (0.6)	27 (0.7)	18 (0.8)	0.78
12-month readmission	404 (34.2)	1,693 (33.3)	1,466 (36.2)	858 (38.1)	<0.01

Data are presented as number(percentage). MACE = major adverse cardiovascular event. MI = myocardial infarction. TVR = target vessel revascularization. CVA = cerebrovascular accident.



Kaplan-Meier Survival Curves

142x103mm (300 x 300 DPI)

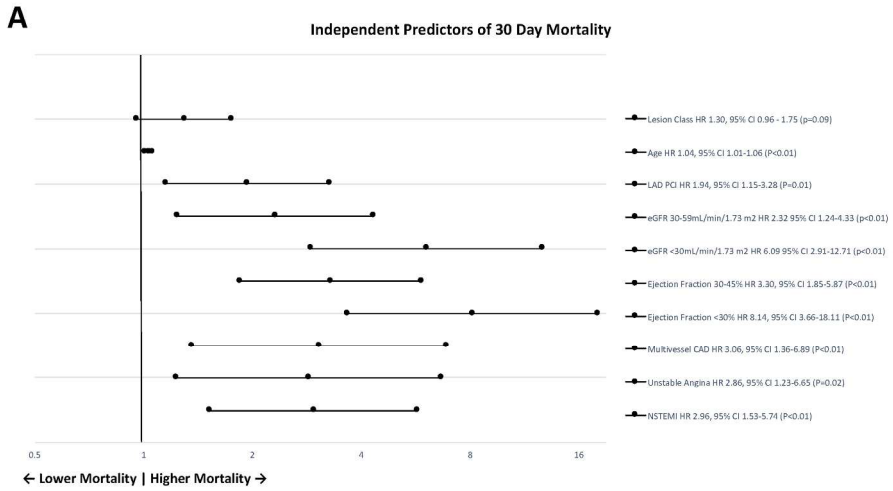


Figure 2A. Independent predictors of 30 day mortality

338x190mm (300 x 300 DPI)

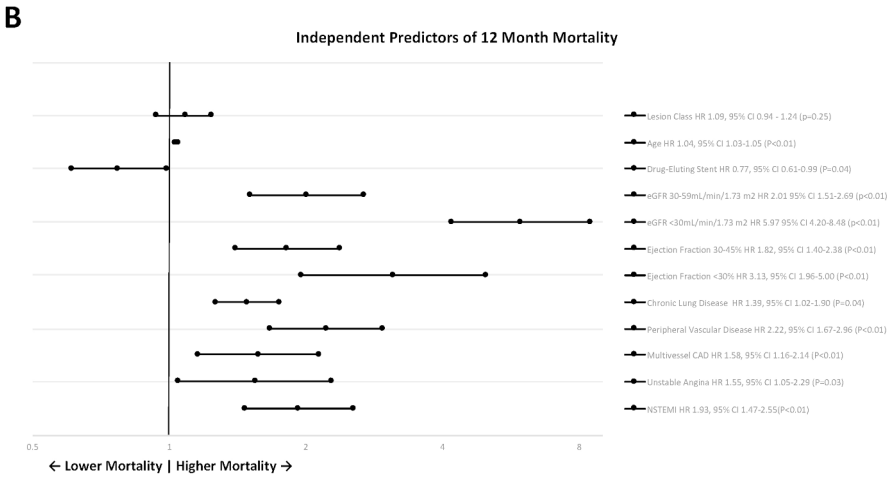


Figure 2B. Independent predictors of 12 month mortality

338x190mm (300 x 300 DPI)

Utility of the ACC/AHA Lesion Classification As a Predictor of Procedural, 30-day and 12-month Outcomes in the Contemporary Percutaneous Coronary Intervention Era

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Keywords: Lesion complexity, PCI, clinical outcomes
Word Count: 3,199 words.
Running Head: Utility of ACC/AHA lesion classification in contemporary PCI

ABSTRACT

Background:

Correlations between the ACC/AHA coronary lesion classification and clinical outcomes in the contemporary percutaneous coronary intervention (PCI) era are not well established.

Methods:

We analyzed clinical characteristics and outcomes according to ACC/AHA lesion classification (A, B1, B2, C) in 13,701 consecutive patients from the Melbourne Interventional Group (MIG) registry. Patients presenting with STEMI, cardiogenic shock and out-of-hospital cardiac arrest were excluded. The primary endpoints were 30-day and 12-month mortality. Secondary endpoints were procedural success as well as 30-day and 12-month major adverse cardiac events.

Results:

Of the 13,7016,249 lesions patients treated, 11,246 (9.1%) had type A lesions, 5,519 (40.3%) had type B1 lesions, 4,449 (32.5%) had Type B2 lesions and 2,487 (18.2%) had Type C ,335 (8.2%) were type A lesions, 6,290 (38.7%) were type B1 lesions, 5,491 (33.8%) were type B2 lesions and 3,133(19.3%) were type C lesions. Patients with type C lesions were more likely to be older and have impaired renal function, diabetes, previous myocardial infarction, peripheral vascular disease and prior bypass graft surgery (all p<0.01). They were also more likely to require rotational atherectomy, drug-eluting stents and longer stent lengths (all p<0.01). Increasing lesion complexity was associated with lower procedural success (99.6% vs. 99.1% vs. 96.6% vs. 82.7%, p<0.001) and worse 30-day (0.2% vs. 0.3% vs. 0.7% vs. 0.6%, p<0.001) and 12-month mortality (9.22.2% vs. 2.0 9.9% vs. 12.93.2% vs. 16.52.9%, p <0.0011). Kaplan Meier analysis showed complex lesions (type B2 and C) had lower survival at 12-months (p=0.003).

Conclusions:

PCI to more complex lesions continues to be associated with lower procedural success rates as well as inferior medium-term clinical outcomes. Thus the ACC/AHA lesion classification should still be calculated pre-procedure to predict acute PCI success and clinical outcomes.

INTRODUCTION

In 1988, the American College of Cardiology and the American Heart Association (ACC/AHA) developed a lesion morphology classification scheme to identify patients most suitable for percutaneous coronary intervention (PCI) with the highest likelihood of procedural success [1, 2]. Consequently, it also identified those at high risk for acute complications.

Historically, lesions are classified across a 3-tier system (A, B and C) based on 11 morphological characteristics. An early modification dividing the intermediate category into B1 and B2 at present time widely accepted [3]. Currently, a binary classification is often employed with A or B1 lesions denoted as "simple", and B2 or C lesions being "complex".

This classification is well validated in percutaneous coronary angioplasty (PTCA) [3], directional atherectomy [4] and rotational atherectomy [5]. In addition, higher lesion complexity using the simplified binary cut-offs has been linked with a poorer prognostic outcome following bare-metal stent deployment [6] and in PCI for acute coronary syndromes [7]. However, these results were challenged by a number of later studies that reported no significant difference in complication rate amongst type A, B and C lesions [8-10]. Furthermore, in a contemporary PCI context Khattab and colleagues showed no prognostic difference between simple and complex lesions in the medium term for patients who received coronary revascularization with sirolimus-eluting stents [11].

Given the conflicting nature of the contemporary data available, the aim of this study was to assess the suitability of the ACC/AHA coronary lesion criteria as a predictor of procedural success, in-hospital complications as well as 30-day and 12-month clinical outcomes in the modern PCI era.

METHODS

A cohort of 13,701 consecutive patients undergoing PCI between 2005 and 2013 were included in our study. A total of 16,249 lesions were treated. All were registered with the Melbourne Interventional Group (MIG), a collaborative consortium of interventional cardiologists practising across 6 major tertiary hospitals in Victoria, Australia [12, 13]. Case reports forms detailing demographic, clinical, procedural and in-hospital outcome data are prospectively collected using standardized definitions and post-procedural outcomes are assessed at 30 days and 12 months.

The MIG registry is coordinated by the Centre of Cardiovascular Research and Education in Therapeutics; an independent research body within the School of Public Health and Preventive Medicine at Monash University (Melbourne, Australia). An audit of a number of verifiable fields from 5% of randomly selected procedures at each institution is undertaken periodically [14]. In the most recent audit, 27 fields were assessed with data accuracy of 98%. This compares favourably to audits from other large registries [15]. The ethics committee in each participating hospital has approved the MIG registry, including the use of "opt-out" consent. This means that consent is presumed unless the patient "opts out". All participating sites give each patient a "Patient Information Sheet". If a patient informs a staff member that they do not wish to participate, the patient's data are not collected.

Patients were stratified according to the ACC/AHA classification criteria as either A, B1, B2 or C (Table 1) [3, 16]. At the time of PCI, a qualified interventional cardiologist classified the lesion being treated. Lesions graded as either A or B1 were considered simple, while those assessed as B2 or C were complex.

Patients presenting with either ST-elevated mycocardial infarction (STEMI), cardiogenic shock or out-of-hospital cardiac arrest were excluded from this study.

The primary endpoints were 30-day and 12-month mortality. Secondary endpoints were acute procedural success and in-hospital complications as well as 30-day and 12-month major adverse cardiac events (MACE). MACE was defined as a combination of mortality, myocardial infarction, and target vessel revascularization. Acute complications included coronary dissection or perforation, in-hospital death, peri-procedural myocardial infarction (MI), cardiac tamponade, cardiogenic shock,

stroke, bleeding, emergency PCI, and unplanned coronary artery bypass grafting (CABG). Procedural success was defined as: <50% residual stenosis for angioplasty or <20% residual stenosis for a stented lesion. Bleeding was defined as a drop of haemoglobin >3.0gm/dl and/or blood transfusion requirement and/or prolonged hospital stay due to bleeding. A stroke is defined by a persistent loss of neurological function (lasting at least 24 hours) caused by an ischaemic or haemorrhagic event, confirmed by CT scan. Clinical criteria for cardiogenic shock were: hypotension (a systolic blood pressure of ≤90 mmHg for at least 30 minutes or the need for supportive measures to maintain a systolic blood pressure of ≥90 mmHg); end-organ hypoperfusion (cool extremities or a urine output ≤30ml/h and a heart rate ≥60 beats per minute); or cardiac index of ≤2.2 L/min per square meter of body-surface area and a pulmonary capillary wedge pressure ≥15 mmHg. Emergency PCI was defined as an unplanned PCI during hospitalization and prior to discharge, which occured as a complication of the index PCI, such as stent thrombosis or dissection with target vessel occlusion.

Statistical analyses were performed using Stata 13.1 (StataCorp LP, College Station, TX, USA). Continuous variables are expressed as mean ± standard deviation (SD), and categorical data are expressed as numbers/percentages. Continuous variables were compared using the Kruskal-Wallis equality-of-populations rank test. Categorical variables were compared using Fisher's exact or Pearson's chi-square tests as appropriate. P values less than 0.05 were considered statistically significant. Cumulative incidence of mortality was estimated by the Kaplan-Meier method and the log-rank test was used to evaluate differences between groups. Cox proportional hazard modelling was used to identify univariate and multivariate predictors of 30-day and 12-month mortality. Univariate variables with a p-value ≤0.10 ~~–~~were tested for evidence of collinearity using pairwise Pearson's correlation coefficient and Variance Inflation Factor. If evidence was found, what we considered the more clinically relevant variable was selected. All remaining variables were then included in a backward selection process to determine the relevant multivariate models~~were included in multivariate models~~. The variables used were: lesion classification, age, sex, eGFR, smoking history, hypertension, diabetes, hypercholesterolaemia, family history of coronary disease, previous MI, previous PCI, previous CABG, heart failure, peripheral vascular disease,

cerebrovascular disease, left ventricular ejection fraction, multivessel CAD, angina type, chronic lung disease, obstructive sleep apnea, rheumatoid arthritis, glycoprotein IIb/IIIa use, drug-eluting stent use, long stent (>20mm), small diameter (<2.5mm), treated lesion location (ostial, bifurcation, left main, LAD, circumflex, right coronary artery, bypass graft) ~~, transient or persistent no reflow~~ and chronic total occlusion.

RESULTS

Baseline Characteristics

13,701 patients were enrolled in the study with 16,249 lesions undergoing PCI. There were 1,335 (8.2%) with type A lesions, 6,290 (38.7%) with type B1, 5,491 (33.8%) with type B2 and 3,133 (19.3%) with type C. Demographic and baseline clinical characteristics are tabulated in Table 2. The cohort was predominantly male (74.6%) with a mean age of 65.2±11.6 years. There was a graded increase in the percentage of patients with diabetes, previous MI, previous PCI/CABG, peripheral vascular disease, cerebrovascular disease, renal impairment (eGFR<30ml/min/1.73m^2), reduced left ventricular ejection fraction (<30%) and multi-vessel CAD with increasing lesion complexity (all $p < 0.01$).

Procedural Characteristics

Table 3 outlines procedural and lesion characteristics. Patients with increasingly complex lesions were more likely to undergo left main PCI, IVUS guidance and rotational atherectomy (all $p < 0.001$). Furthermore, the more complex lesions required larger calibre guiding catheters, longer stent lengths and received a much higher proportion of drug-eluting stents. Chronic total occlusions made up 23.5% of type C lesions, respectively.

In-Hospital Complications and Clinical Outcomes

In-hospital complications and outcomes are outlined in Table 4. There was an inverse relationship between lesion complexity and procedural success. Furthermore, as lesion complexity increased there was a significant increase in peri-procedural complications including coronary dissection and perforation, peri-procedural myocardial infarction, no re-flow, cardiogenic shock and unplanned CABG (all p value for trend <0.01). There was no significant difference between lesion classes with regards to urgent PCI, stroke, in-hospital major bleeding and mortality.

Mortality at 30 days was highest in those with complex lesions (A 0.2%, B1 0.3%, B2 0.7% and C 0.6%; $p < 0.01$; Table 5) and this trend was maintained at 12 months (A 2.2%, B1 2.0%, B2 3.2% and C 2.9%; $p < 0.01$; Table 5). MI, TVR and MACE were also progressively higher with increasing lesion complexity at both 30 days and 12 months (Tables 5).

Kaplan Meier survival curve shows a significantly worse 12-month survival in patients with complex lesions (p = 0.003, Figure 1). Multivariate predictors of 30-day and 12-month mortality are shown in Figure 2.

DISCUSSION

Three important conclusions can be drawn from this study regarding the modified ACC/AHA lesion morphology classification scheme and its application in the contemporary PCI era. Firstly, ACC/AHA classification remains a strong predictor of procedural success and there were higher rates of unsuccessful PCI with increasingly complex lesions. Secondly, more complex lesions were associated with higher rates of multiple in-hospital complications, including coronary artery dissection, vessel perforation, myocardial infarction, cardiogenic shock and unplanned CABG. Lastly, higher lesion complexity correlated with higher mortality rates and major adverse cardiovascular events at both 30-days and 12-months.

In the coronary angioplasty era, Ellis and colleagues [3] demonstrated markedly lower success rates and increasing complications with higher degrees of lesion complexity. In comparison, the much higher procedural success rates seen in our study (A lesion: 99.6% vs. 92%, B1 lesion: 99.1% vs. 84%; B2 lesion: 96.6% vs. 76%; C lesion: 82.7 vs. 61%) highlights the improvement in PCI techniques and performance over the past three decades. What has remained constant is the stepwise decrease in success rates across the lesion classification categories. Similarly, while overall complication rates have decreased, they are still proportional to lesion complexity. This has implications for informed consent of patients prior to PCI. Zaacks and colleagues [8] found that specific lesion characteristics, namely total occlusions and tortuosity, rather than ACC/AHA lesion classification to be predictive of complications but this study was limited by small sample size. We included tenfold more patients and this greater power has allowed us to discriminate across the four lesion classification categories, in spite of the low numbers of unsuccessful procedures and complications in contemporary PCI. Our data therefore reinforces the utility of lesion classification at time of PCI to assess success rate and complication risk.

Modern PCI techniques, improved equipment and the availability of optimal pharmacotherapy have been postulated as reasons for the diminished predictive ability of lesion classification [8-11]. Utilization of these advances in interventional cardiology was evident in our cohort of patients, particularly in those with complex lesions as they were more likely to be treated with rotational atherectomy, drug-eluting stents and glycoprotein IIb/IIIa inhibitors, along with higher rates of IVUS-guided PCI. While the

greater use of these newer technologies were associated with significant improvement in procedural outcomes in our study, they do not completely eliminate the risk posed by more complex lesions. It is also worth considering that the advancement in technology may also increase the complexity of lesions having attempted PCI, such as chronic total occlusion.

Kastrati and colleagues found the short- and medium-term prognostic value of the ACC/AHA lesion classification was preserved in PCI in an observational study with bare-metal stents [6]. However, Khattab *et al.* did not find a significant difference in death, myocardial infarction and target vessel revascularisation between simple and complex lesions following PCI with 1st generation sirolimus-eluting stents, although a trend towards increased myocardial infarction and death in complex lesion patients was identified [11]. In comparison with these studies, the main advantage of our study is its larger population and the use of the complete ACC/AHA classification rather than the dichotomy of simple vs. complex lesion. Furthermore, our study is a more robust representation of contemporary PCI as we included consecutive patients irrespective of initial procedural success whereas the German Cypher Registry used in Khattab *et al* [11] only included patients where a sirolimus-eluting stent was successfully deployed. Although a successfully treated complex lesion may have similar clinical outcomes to a simple lesion, it does not diminish the prognostic value of the lesion classification to predict procedural success. Indeed, our study strengthens the contention that the ACC/AHA lesion classification translates beyond procedural success and also predicts medium term-clinical outcomes.

It is plausible that lesion complexity may be a marker of more advanced atherosclerosis. We have shown that patients with increasingly more complex lesions are more likely to have a history of previous MI, PCI, CABG and higher rates of both multi-vessel coronary artery disease and peripheral vascular disease. They also have a higher burden of co-morbidities, namely diabetes mellitus, chronic renal impairment and left ventricular dysfunction. This is consistent with previous studies [3, 6, 11]. While these co-morbidities may partially explain the worse outcomes with more complex lesions, the fact remains that lesion class is closely linked to short- and medium term MACE in contemporary PCI and lesion classification remains a predictor, albeit modest, of 30-day mortality.

Our study has several limitations that warrant discussion. First and most importantly, inter-operator variability exists in assessing coronary lesion morphology according to the ACC/AHA classification system and independent external assessment of coronary angiograms was not performed. Variation by one classification has been observed in over 30% of cases in a previous study, however variation by two classifications (eg. B1 lesion classified as a C lesion) is rare [3]. Secondly, given the retrospective nature of our study there may be unaccounted factors that influence procedural decision-making and outcomes. Thus our results are hypothesis generating rather than conclusive. Thirdly, we do not capture details of interventional methods thus we cannot account for advancements in chronic total occlusion and bifurcation techniques as well as the availability of newer equipment.

CONCLUSION

The present study confirms that the ACC/AHA lesion morphology classification remains an important predictor of procedural success, in-hospital complications and medium term-outcomes. Thus it should still be an important part of risk-benefit assessment and informed consent of patients prior to PCI.

Figure 1. Kaplan-Meier Survival Curves

Figure 2. Independent Predictors of 30 Day and 12 Month Mortality

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Acknowledgements:

The Melbourne Interventional Group acknowledges unrestricted educational grant funding from: Abbott Vascular, Astra-Zeneca, Medtronic, MSD, Pfizer, Servier, and The Medicines Company. These companies do not have access to the data, and do not have the right to review manuscripts before publication.

Dr. Yudi is supported by a combined National Health and Medical Research Council Postgraduate Scholarship (APP 1115163) and a National Heart Foundation Health Professional Scholarship (Award ID 101130). Dr. Duffy's & Professor Reid's work is funded by National Health and Medical Research Council of Australia Grants.

The Melbourne Interventional Group acknowledges and thanks all patients who have been involved in the registry.

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