Safety of Rotational Atherectomy Using the Radial Access in Patients With Severe Aortic Stenosis

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Despite frequent percutaneous coronary intervention (PCI) in calcified vessels of older patients, rotational atherectomy (RA) has not been endorsed in patients with severe aortic stenosis (AS) due to safety concerns and lack of data. We explored periprocedural safety and mortality in severe AS patients undergoing RA. Prospective anonymized clinical, echocardiographic, procedural and outcome data of patients undergoing RA PCI between January 2012 and July 2018 were retrospectively extracted from the institutional coronary database. Patients with severe AS undergoing RA PCI were 1:1 propensity matched with patients undergoing RA PCI in the absence of AS. Outcomes of interest were RA related periprocedural complications, 30-day and 1-year mortality. A prespecified subgroup analysis examined the influence of transcatheter aortic valve replacement on mortality following RA PCI. A total of 544 patients underwent RA PCI; 478 without AS and 66 with AS. Propensity matching yielded 35 matched pairs with improved balance in covariates of interest and no significant differences in baseline characteristics postmatching. In the matched cohort (n = 70) slow flow/no-reflow, coronary dissection, perforation, and hemodynamic instability were rare and not significantly different. Survival analyses revealed significantly higher 30-day (Log-Rank p = 0.02) and 1-year mortality (Log rank p = 0.02, HR 5.24 [95% CI 1.13 to 24.28]) in the severe AS group; driven by a fivefold increase in the hazard of death among patients who did not undergo transcatheter aortic valve replacement HR 4.98 [95% CI 1.03 to 24.1]. In conclusion, our study of 70 patients undergoing radial RA PCI suggests that it can be safely performed in patients with severe AS. Long-term outcomes after RA in patients with severe AS are determined by the presence of the valve disease and other co-morbidities. **(Am J Cardiol 2019;124:381−388)**

Rotational atherectomy (RA) facilitates percutaneous coronary intervention (PCI) of severely calcified and often complex coronary lesions.[1] Coronary artery disease in elderly patients with severe aortic stenosis (AS) ranges from 50% to 75% [2,3] with complex, calcified coronary lesions reported in 10% to 30% of transcatheter aortic valve replacement (TAVR) patients.[4,5] Since the introduction of TAVR for high surgical risk elderly patients, complex, calcified coronary lesions amenable to RA facilitated PCI are frequently encountered during preoperative coronary angiography.[4,5] However, RA is not routinely performed in severe AS patients due to concerns about slow-flow/no-reflow and dissection that may lead to hemodynamic decompensation and poor outcomes.[1,6] To date, safety data for rotational atherectomy in severe AS patients is scant and confined to case reports and case series.[7−10] Our study explores the procedural safety of RA facilitated PCI in severe AS patients, subsequent early and late mortality, and compares them to procedural outcomes and mortality of patients who undergo RA in the absence of severe AS.

Methods

All patients undergoing rotational atherectomy PCI at the Oxford Heart Centre between January 2012 and July 2018 were registered in the institutional interventional database. Prospectively collected anonymized clinical, procedural and outcome data were extracted from a centrally administered and managed database under audit authorization No 5165 from the Oxford University Hospitals NHS Trust. Individual patient consent was not sought as anonymized and prospectively collected data were analyzed in the study.

Data on demographic characteristics, hypertension, hypercholesterolemia, peripheral arterial disease (PAD), AS, smoking status, previous cerebrovascular accident, previous myocardial infarction, previous PCI, left ventricular ejection fraction (LVEF) and creatinine levels were extracted. Routinely reported echocardiogram data in RA patients with AS were also collected and used to classify the severity of AS according to ACC/AHA guidelines.[11] TAVR was ascertained

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See page 387 for disclosure information.

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by interrogation of the database, censored to December 2018. Coronary angiograms were independently reviewed by 2 interventional cardiologists for lesion characterization, procedural characteristics, and complications.

Radial access with a sheathless guiding catheter has been the default strategy in our institution.[12] Following engagement of the coronary artery with a guiding catheter, a Rotawire (Boston Scientific, Maple Grove, MN) was advanced to the distal third of the coronary artery. The smallest burr size deemed by the operator sufficient to modify the plaque was chosen; maintaining a burr-artery ratio of <0.6. Ablations were performed with the Rotablator System (Boston Scientific) for <20 seconds in duration at 140,000 to 160,000 rotation per minute without infusion of a proprietary rotablation "cocktail" and minimizing the use of vasodilators. Following successful lesion modification, drug eluting stents were implanted when clinically indicated. Imaging optimization and postdilation were performed at the discretion of experienced operators. Elective right ventricle temporary pacing is not routinely used during right coronary artery RA cases in our institution.

Periprocedural outcomes including intraprocedural death, ventricular tachycardia/ ventricular fibrillation, pericardial effusion, coronary perforation, dissection, slow flow/no reflow and hemodynamic instability were identified through review of coronary angiograms and procedural reports by two independent interventional cardiologists. A composite safety end point including hierarchically the aforementioned periprocedural outcomes was defined a priori. Thirty day and 1-year mortality data are prospectively collected and regularly updated as our institutional coronary database is linked to NHS spine (NHS digital). The mortality data presented herein were censored to December 2018.

Normality assumption was tested by visual inspection and statistically by Shapiro-Wilk and Kolmogorov-Smyrnov testing. Normally distributed continuous variables were reported as mean ± standard deviation, with non-normally distributed data reported as median [interquartile range]. Categorical variables were summarized as count and frequency. Between group differences in continuous variables were evaluated with the Student's *t* test or Mann-Whitney U test as appropriate. Comparisons between categorical variables were performed using the Fisher's exact test or the Pearson's chi-square test, as appropriate. Missing data were excluded from inferential statistical analyses.

A propensity score for the probability of assignment to rotational atherectomy in severe AS was derived using a multivariate regression model. Variables included age and poor LVEF (≤30%) − established predictors of poor outcome in RA[13,14] − as well as gender and procedural urgency. One-to-one propensity matching without replacement and nearest neighbor matching was performed. Confounders included in the propensity model were compared before and after matching qualitatively by inspection of box-plots and statistically using absolute standardized differences. Sufficient balance was defined when absolute standardized difference after matching was <20%.[15]

After matching, categorical outcomes were compared using either Fisher's exact test, or McNemar's binomial test as appropriate. Time to event outcomes were compared between treatment groups using Kaplan-Meier survival analysis and Cox Regression Models. A prespecified sensitivity analysis to investigate the influence of TAVR for severe AS on mortality within a year from RA was also performed. Landmark analyses were performed to explore influence of periprocedural death on mortality. All analyses were performed using SPSS 24.0 (IBM Inc. New York). The cut-off for statistical significance was set at $p < 0.05$.

Results

During the index period, 544 patients met the inclusion criteria with 66 having an underlying diagnosis of AS. Following analysis of echocardiographic data, 17 patients were found to have moderate AS at the time of RA and therefore excluded from the analysis (Figure 1). Echocardiograph parameters of 49 patients with severe AS are presented in Table 1.

Prior to matching, significant differences were observed in age, body mass index (BMI), smoking history, PAD, renal function and LVEF (Table 2). Patients undergoing RA without AS were younger, with a higher prevalence of smoking and PAD. Patients with severe AS undergoing RA had lower BMI, worse renal, and LV function. Following propensity matching, baseline differences were abolished yielding two more homogeneous groups (Table 2).

RA was performed for severe proximal calcific disease or angina refractory to medical treatment. Radial access was more common and a sheathless guide catheter was used in all

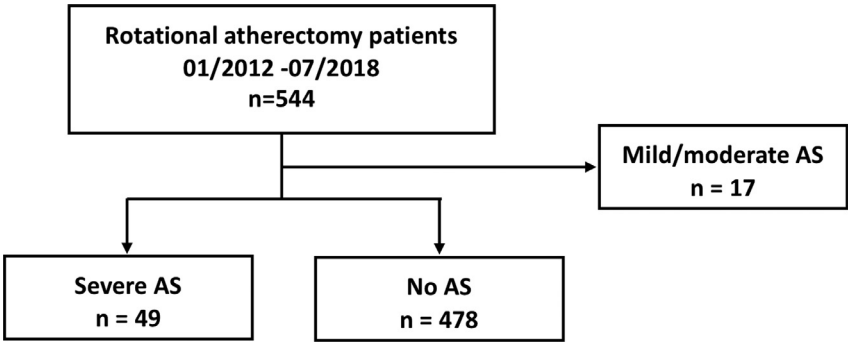

Figure 1. Study flow diagram.
AS = aortic stenosis.

Table 1
Echo characteristics of severe aortic stenosis cohort

Variable	Rotational atherectomy in severe aortic stenosis
Aortic valve area (cm^2)	0.72 (0.60, 0.94)
Indexed aortic valve area (cm^2/m^2)	0.40 (0.32, 0.51)*
Peak transvalvular gradient (mmHg)	64 (23)
Mean transvalvular gradient (mmHg)	37 (14)

Continuous data are reported as mean (standard deviation) or median (first quartile, third quartile).
* n = 2 values missing.

transradial procedures (Table 3). Lesion profile details are presented in Table 3. Screening time, contrast utilization and procedural complications, were not significantly different between the two groups (Tables 3 and 4, Figure 2). One intra-procedural death occurred in a severe AS patient who developed significant hemodynamic instability due to no reflow prior to lesion predilatation. One patient developed significant hemodynamic instability during transient slow-flow following rotational atherectomy.

Median follow-up was 365 days with 2 patients censored at 311 and 304 days. A trend toward higher 30-day mortality was observed in patients with severe AS undergoing RA when compared with patients without severe AS undergoing RA (14% vs 0%, p = 0.05, Table 4). Kaplan-Meier survival analysis revealed a significant difference between the 2 groups (Log-Rank Chi-square 5.3, p = 0.02) (Figure 3). All deaths were from cardiovascular causes (Suppl. Table 1).

At 1-year follow-up, mortality was significantly higher among severe AS patients undergoing RA (26% vs 6%, p = 0.02, HR 5.24 [95% CI 1.13 to 24.28], p = 0.03, Table 4). Survival analysis corroborates the significant difference among the 2 groups (Log-Rank Chi-square 5.6, p = 0.02) while showing that survival curve separation was evident during the first 50 days but did not expand thereafter (Figure 3). Mortality was driven by cardiovascular causes in all patients with available cause of death (Suppl. Table 1). Landmark analyses excluding periprocedural death(s) did not change the significance of observed effects.

A prespecified subgroup analysis was performed to probe the influence of TAVR within a year from RA on mortality. The matched cohort was split into 3 groups of patients; patients with no severe AS (n = 35), patients with severe AS who did not proceed to TAVR within a year (n = 16), and patients with severe AS who underwent TAVR within a year (n = 19). Severe AS cases were discussed at the "Heart Team" multidisciplinary meeting to establish clinical eligibility for TAVR. Median time to TAVR was 85 (57, 149) days. Baseline characteristics were not significantly different among groups (Suppl. Table 2). Kaplan-Meier analyses identified significant differences in the 30-day and 1-year survival probabilities among the 3 groups (Figure 4), that persisted in landmark analyses excluding periprocedural death(s).

Cox regression models using patients without severe AS as the reference standard found no difference in 30-day mortality among the 3 groups. The 1-year survival probability of RA patients who had TAVR was not significantly

Table 2
Baseline characteristics before and after propensity matching

Variable	Before matching				After matching			
	Overall (n = 527)	Rotational atherectomy and no aortic stenosis (n = 478)	Rotational atherectomy in severe aortic stenosis (n = 49)	p value	Overall (n = 70)	Rotational atherectomy and no aortic stenosis (n = 35)	Rotational atherectomy in severe aortic stenosis (n = 35)	p value
Age (years)	76 (70, 82)	76 (69, 82)	82 (79, 87)	<0.01	81 (6)	80 (6)	81 (5)	0.67
Women	131 (25%)	120 (25%)	11 (22%)	0.68	17 (24%)	8 (23%)	9 (26%)	0.78
Hypertension	476 (90%)	432 (90%)	44 (90%)	0.80	62 (89%)	30 (86%)	32 (91%)	0.45
Hypercholesterolemia	398 (76%)	361 (76%)	37 (75%)	1.00	53 (76%)	26 (74%)	27 (77%)	0.78
Diabetes mellitus	152/509 (30%)	141/460 (31%)	11 (22%)	0.23	17 (25%)	9/34 (27%)	8 (23%)	0.73
Smoker	362/520 (69%)	339/472 (72%)	22/48 (46%)	<0.01	40 (57%)	23 (58%)	17 (43%)	0.15
Peripheral arterial disease	119 (23%)	114 (24%)	5 (10%)	0.03	12 (17%)	8 (23%)	4 (11%)	0.21
Previous cerebrovascular accident	46 (9%)	43 (9%)	3 (6%)	0.79	7 (10%)	5 (14%)	2 (6%)	0.23
Previous myocardial infarction	121/474 (26%)	111/426 (26%)	10/48 (21%)	0.43	18/64 (28%)	10/30 (33%)	8/34 (24%)	0.39
Previous percutaneous coronary intervention	184/519 (36%)	171/471 (36%)	13/48 (27%)	0.20	22/68 (32%)	13/34 (38%)	9/34 (27%)	0.30
Creatinine (mmol/L)	89 (75, 115)	88 (75, 113)*	101 (84, 131)	0.04	98 (84, 129)	99 (85, 119) †	96 (84, 132)	0.99
Left ventricular ejection fraction (%)	50 (45, 55)	50 (45, 55)	50 (35, 50)	0.04	50 (45, 55)	50 (45, 55)	50 (45, 50)	0.18
Poor left ventricular ejection fraction	39 (7%)	29 (6%)	10 (20%)	<0.01	2 (3%)	1 (3%)	1 (3%)	1.00

Continuous data are reported as mean (standard deviation) or median (first quartile, third quartile).
* n = 37 values missing;
† n = 3 values missing.

Table 3
Angiographic analyses of propensity matched cohorts

Variable	Overall	Rotational atherectomy and no aortic stenosis	Rotational atherectomy in severe aortic stenosis	p value
Number of lesions	72	35	37	-
Coronary narrowing location				0.03*
Left main	18 (25%)	11 (31%)	7 (19%)	
Left anterior descending	24 (33%)	8 (23%)	16 (43%)	
Left circumflex	13 (18%)	10 (29%)	3 (8%)	
Right	17 (24%)	6 (17%)	11 (30%)	
Lesion characterization				
Diameter stenosis (%)	78 (65, 80)	80 (70, 80)	70 (63, 83)	0.29
Diameter stenosis by quantitative coronary angiography (%)	51 (40, 61)	53 (45, 70)†	49 (40, 58)	0.32
Lesion length (mm)	14 (10, 25)	11 (9, 26)†	15 (10, 28)	0.38
Bifurcation	33 (46%)	17 (49%)	16 (43%)	0.65
Chronic total occlusion	2 (3%)	2 (6%)	0	0.23
Ambrose classification B2/C	64 (90%)	31 (89%)	34 (92%)	0.71
Procedural data				
Radial access	59 (84%)	29 (83%)	30 (86%)	0.74
Burr size (mm)	1.5 (1.5, 1.75)‡	1.5 (1.5, 1.75)	1.5 (1.75, 1.75)	0.62
Burr upsizing	5 (7%)	2 (6%)	2 (6%)	1.00
Predilatation	71 (99%)	34 (97%)	37 (100%)	0.49
Cutting balloon	2 (3%)	1 (3%)	1 (3%)	1.00
Total stent length (mm)	32 (20, 49)§	33 (22, 54)	32 (20, 47)	0.36
Postdilatation	69 (96%)	33 (94%)	36 (97%)	0.61
Imaging optimized	9 (13%)	3 (9%)	6 (8%)	0.48
Use of GpIIb/IIIa	2 (3%)	2 (6%)	0	0.49
Procedure time (min)	65 (28)‖	63 (28)	66 (29)	0.68
Screening time (min)	15 (10, 19)¶	17 (11, 24)	13 (10, 17)	0.06
Contrast (ml)	160 (130, 210)#	170 (135, 218)	160 (128, 206)	0.49

Continuous data are reported as mean (standard deviation) or median (first quartile, third quartile).
* not statistically significant in post-hoc analysis with Bonferroni correction;
† n = 14 values missing;
‡ n = 4, 1 in the rotational atherectomy and no aortic stenosis group, 3 in the rotational atherectomy in severe aortic stenosis;
§ n = 7, 4 in the rotational atherectomy and no aortic stenosis group, 3 in the rotational atherectomy in severe aortic stenosis;
‖ n = 13, 6 in the rotational atherectomy and no aortic stenosis group, 7 in the rotational atherectomy in severe aortic stenosis;
¶ n = 5, 1 in the rotational atherectomy and no aortic stenosis group, 4 in the rotational atherectomy in severe aortic stenosis and
# n = 3, 2 in the rotational atherectomy and no aortic stenosis group, 1 in the rotational atherectomy in severe aortic stenosis.

different to the survival probability of RA patients without severe AS HR 1.96 [95% CI 0.28 to 13.91], p = 0.5. The observed effects on survival are due to a fivefold increase in the hazard of death among patients who did not proceed to TAVR when compared with patients who had TAVR HR 4.98 [95%CI 1.03 to 24.1], p <0.05.

Discussion

To our knowledge, this is the first analysis comparing RA PCI in severe AS against RA PCI in the absence of AS. The results of our propensity matched cohort suggest that RA PCI is procedurally safe in severe AS. It also identifies that patients with severe AS undergoing RA PCI have poor

Table 4
Outcomes of propensity matched cohorts

Variable	Rotational atherectomy and no aortic stenosis	Rotational atherectomy in severe aortic stenosis	p value
Periprocedural death	0	1 (3%)	NS
30-day mortality	0	5 (14%)	0.05
1-year mortality	2 (6%)	9 (26%)	**0.02**
Intraprocedural ventricular tachycardia/fibrillation	0	0	-
Hemodynamic instability	0	2 (6%)	NS
Pericardial effusion	0	0	-
Coronary perforation	0	0	-
Dissection	1 (3%)	1 (3%)	NS
Slow-flow/No-reflow	0	2 (6%)	NS
Composite safety end point	1 (3%)	3(9%)	NS

NS = not significant.

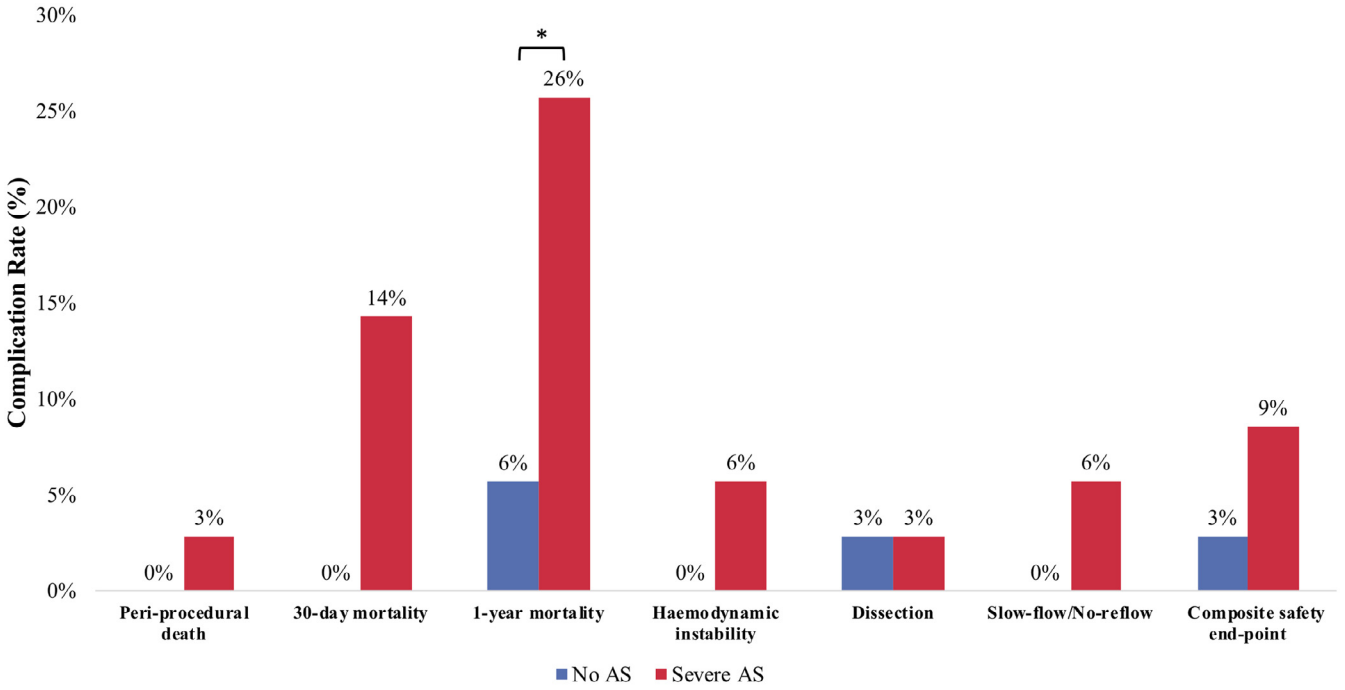

Figure 2. RA PCI complications in patients with severe AS compared with patients with no AS.
AS = aortic stenosis; PCI = percutaneous coronary intervention; RA = rotational atherectomy * denotes a statistically significant difference p <0.05.

1-year survival due to a fivefold increased hazard of death among severe AS patients that do not proceed to AVR.

Since the introduction of TAVR, complex calcified coronary lesions amenable to RA PCI are frequently encountered in pre-TAVR coronary angiography.[4,5] The coronary and/or TAVR teams have to carefully weigh the risks and benefits of PCI.[16] On the one hand, PCI in TAVR patients is associated with increased vascular complications and early

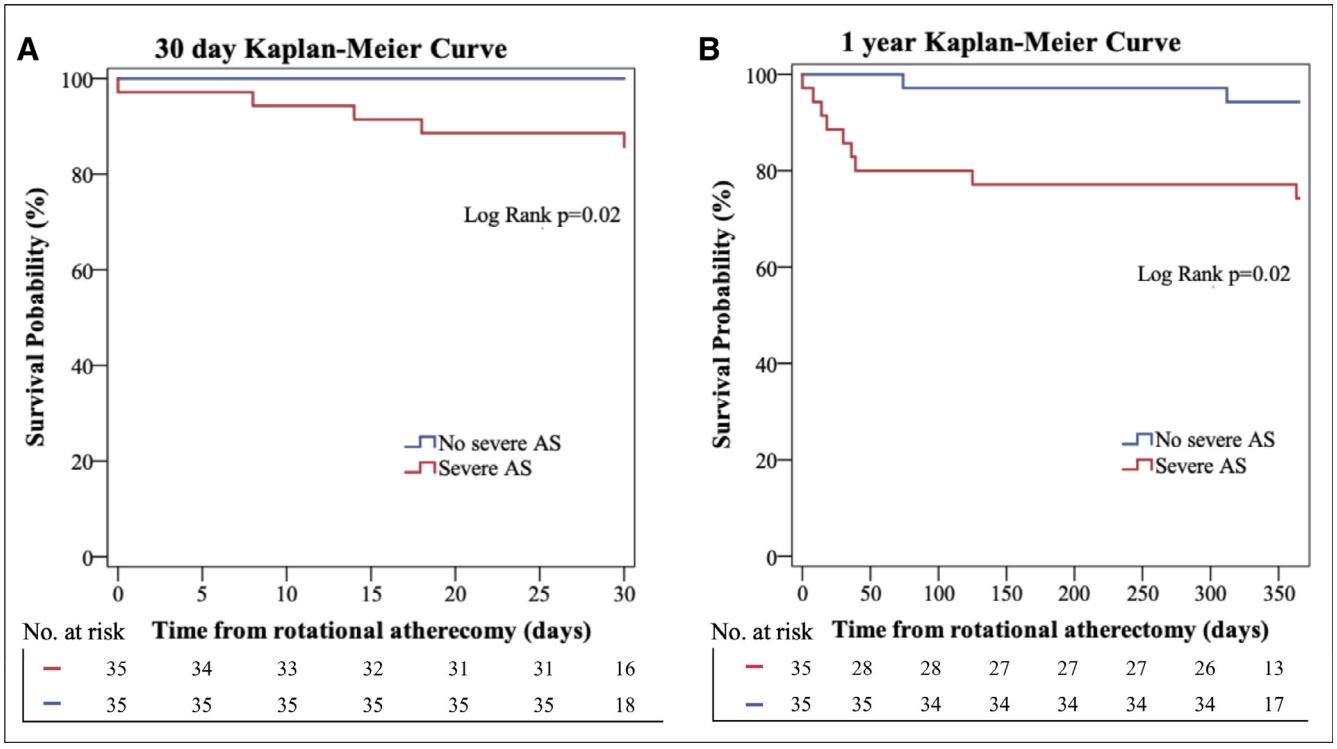

Figure 3. 30-day *(A)* and 1-year *(B)* Kaplan-Meier Curves in patients undergoing RA PCI with severe AS compared with patients without AS.
AS = aortic stenosis.

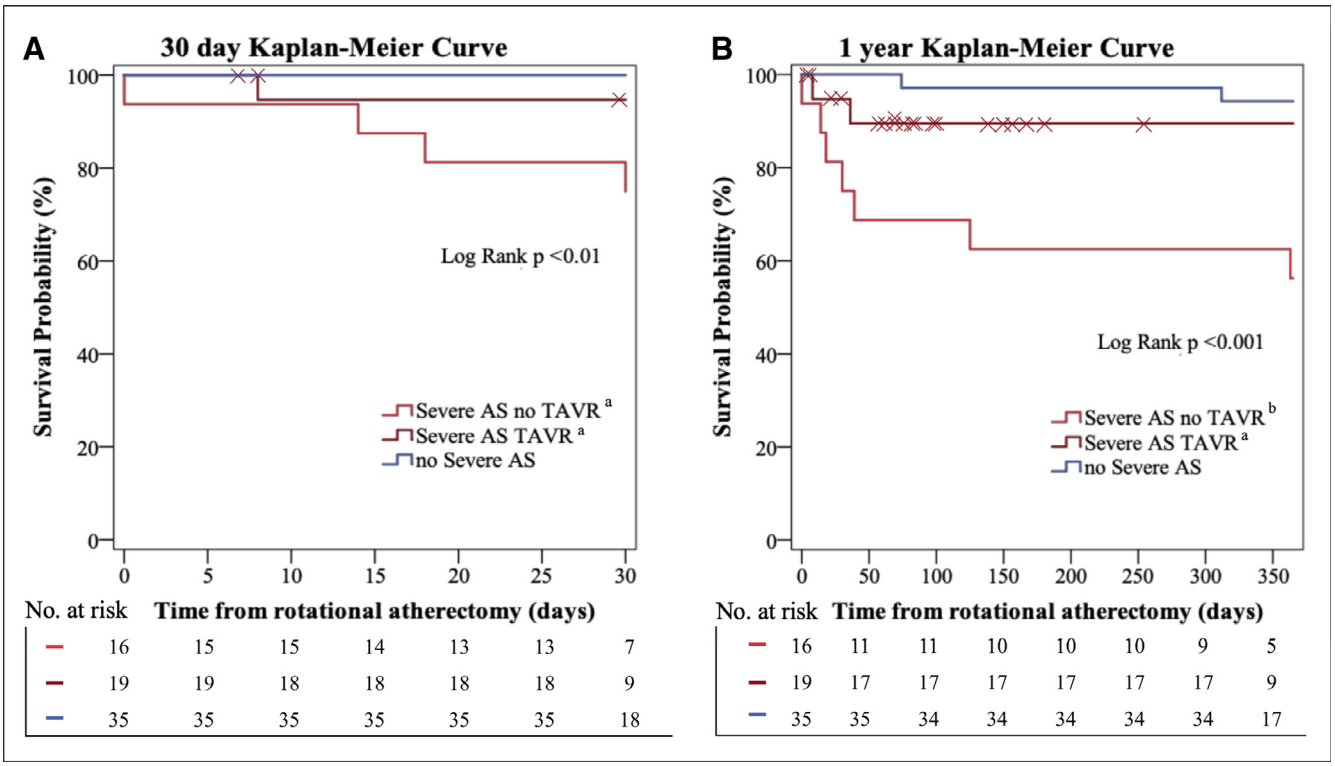

Figure 4. 30-day *(A)* and 1-year *(B)* Kaplan-Meier curves in patients undergoing RA PCI in without AS, in severe AS patients who had TAVR and in patients with severe AS that did not proceed to TAVR. The time of TAVR for each patient is indicated by a cross.
AS = aortic stenosis; PCI = percutaneous coronary intervention; RA = rotational atherectomy; TAVR = transcatheter aortic valve replacement. *(a)* no significant difference when compared with no severe AS group; *(b)* significant difference when compared with no severe AS group.

mortality,[2] while incomplete revascularization increases long-term mortality following TAVR.[17] RA is an important lesion modification strategy that could facilitate PCI of complex calcified lesions; enabling complete revascularization while reducing target-vessel revascularization failure rates.[18] The aforementioned are increasingly important as TAVR is expanding toward younger patients of low/intermediate surgical risk,[19,20] though coronary access following TAVR is feasible.[21]

Despite the potential benefits, RA is not employed in severe AS due to paucity of data and concerns regarding periprocedural complications in patients with impaired LV function.[1] In the PROTECT II trial, RA was associated with poor periprocedural outcome in complex PCI patients requiring hemodynamic support despite the use of LV support devices.[22] A case series of RA in severe AS suggests that transient changes in hemodynamic parameters are common, but do not result in adverse clinical outcomes.[9] In our study, hemodynamic instability was rare; yet numerically higher in patients with severe AS (6% vs 0%), encountered in patients with slow-flow/no-reflow, and responsible for 1 periprocedural death.

Slow-flow/no-reflow – an established RA complication – occurs in 2% to 7% of cases secondary to distal embolization of prothrombotic atherosclerotic debris.[1] The resulting microcirculatory dysfunction can have profound adverse effects, especially in severe AS patients with poor coronary flow reserve and severe LV impairment.[23] High-risk patients may benefit from upfront use of the Diamondback 360 Coronary Orbital Atherectomy System (Cardiovascular Systems Inc., St. Paul, MN) which has been shown to have a lower incidence of slow-flow/no-reflow than RA (0.7% to 4% vs 2% to 7%) and no periprocedural harm signal in patients with impaired LV.[24,25] Alternatively, early clinical studies of the new CE-marked balloon-based Shockwave Coronary Rx Lithoplasty System (Shockwave Medical, Fremont, CA) show no incidence of slow-flow/no-reflow or perforations, rendering it an attractive lesion modification tool in crossable lesions.[26] Finally, appropriate use of mechanical and inotropic support in patients with complications can enhance RA periprocedural safety.[10]

Despite the procedural safety of RA PCI in severe AS, survival analyses identified a trend toward reduced 30-day survival, due to cardiovascular mortality. This effect is likely due to the physiological and functional burden of severe AS. The latter is re-affirmed by the fivefold increase in the hazard of death among severe AS patients at 1 year. Indeed, TAVR may be performed in these patients following a careful individualized review by the Heart Team. Although there appears to be a difference in 1-year survival following TAVR, our analyses should be cautiously interpreted as they are likely confounded by the fact that patients who underwent TAVR following RA PCI may have been physiologically and functionally healthier than those that did not have TAVR. In terms of when TAVR should be performed we visually identify the risk of death following RA PCI in severe AS patients to be higher in the first 50 days.

Our study harbors the limitations of retrospective studies. Firstly, despite our attempt to control for important confounders of the relationships we were exploring through propensity matching; residual confounding may still be present particularly as multivariate analyses were not employed. Secondly, even though this is the first study comparing RA PCI in severe AS patients to patients without AS it is a single center, small size study (n = 70), underpowered to draw definitive conclusions regarding periprocedural complications and hence should be considered as hypothesis-generating. However, the rates of periprocedural complications of RA PCI in severe AS patients were comparable to complication rates in patients undergoing RA PCI in the absence of AS.[1,25] Finally, our study did not explore the reasons behind not proceeding to TAVR in severe AS patients and inferences regarding mortality and time of intervention should be cautiously interpreted and further tested in larger, purpose-designed studies.

In conclusion, in our cohort of 70 patients RA facilitated PCI in severe AS patients is safe in terms of periprocedural complications. Early and late survival amongst severe AS patients undergoing RA PCI is poorer that survival rates of patients without AS; due to the cardiovascular burden of severe AS. Larger scale studies are required to explore predictors of periprocedural complications in patients with severe AS undergoing RA PCI and study the potential of newer devices to modify the risk profile of lesion modification strategies.

Disclosures

Adrian P. Banning reports grants from Boston Scientific, personal fees from Boston Scientific, personal fees from Abbott, personal fees from Medtronic, personal fees from Phillips, outside the submitted work; Rajesh K. Kharbanda reports personal fees from Boston Scientific, during the conduct of the study; Adrian P. Banning & Rajesh K. Kharbanda are partially funded by the NHS NIHR Biomedical Research Centre, Oxford; Rafail A Kotronias's post is funded by the National Institute for Health Research; Roberto Scarsini received an EAPCI Education and Training Grant. The rest of the authors have nothing to declare.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.04.052.

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