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The Modified Arch Landing Areas Nomenclature predicts proximal endograft failure after thoracic endovascular aortic repair

Massimiliano M. Marrocco-Trischitta ^{a,*}, Hector W. de Beaufort ^{a,b}, Gabriele Piffaretti ^c, Stefano Bonardelli ^d, Mauro Gargiulo ^e, Michele Antonello ^f, Joost A. van Herwaarden ^b, Sara Boveri ^g, Raffaello Bellosta ^h, and Santi Trimarchi ^{i,j}, on behalf of the MALAN Collaborators [†]

^a Clinical Research Unit and Division of Vascular Surgery, IRCCS Policlinico San Donato, San Donato Milanese, Italy

^b Department of Vascular Surgery, University Medical Center Utrecht, Utrecht, Netherlands

^c Vascular Surgery, Department of Surgery and Morphological Sciences, Circolo University Teaching Hospital, University of Insubria School of Medicine, Varese, Italy

^d Department of Vascular Surgery, A.O Spedali Civili di Brescia, University of Brescia, Brescia, Italy

^e Vascular Surgery, DIMES, Policlinico Sant'Orsola-Malpighi, University of Bologna, Bologna, Italy

^f Vascular and Endovascular Surgery Division, Padua University, School of Medicine, Padua, Italy

^g Scientific Directorate, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy

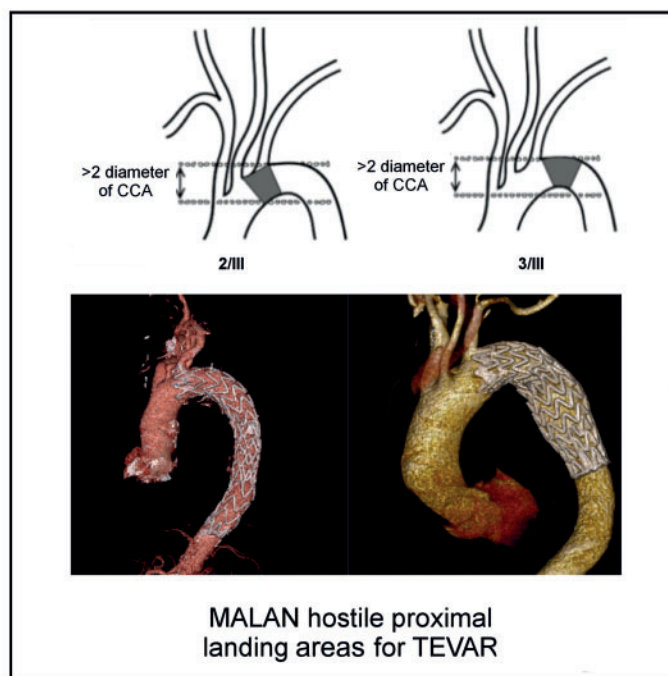
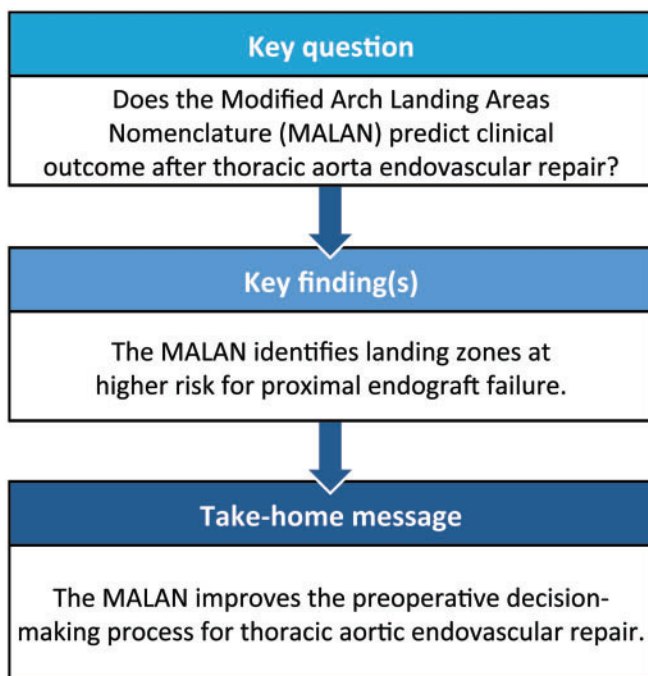
^h Vascular Surgery Unit, Cardiovascular Surgery Department, Poliambulanza Foundation Hospital, Brescia, Italy

ⁱ Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

^j Department of Clinical and Community Sciences, University of Milan, Milan, Italy

* Corresponding author. Clinical Research Unit and Division of Vascular Surgery, Cardiovascular Department, IRCCS Policlinico San Donato, Via Morandi 30, 20097 San Donato Milanese, Italy. Tel. +39-02-52774695; e-mail: massimiliano.marroccotrischitta@grupposandonato.it; max_marrocco@yahoo.com (M.M. Marrocco-Trischitta).

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[†]The members and affiliations of MALAN Collaborators are listed in the Acknowledgements section.

Abstract

OBJECTIVES: Our goal was to assess the value of the Modified Arch Landing Areas Nomenclature (MALAN) for thoracic endovascular aortic repair (TEVAR), in which each landing area (LA) is identified by a proximal landing zone and the type of arch (e.g. 0/I), as predictors of postoperative proximal endograft performance.

METHODS: A multicentre retrospective analysis was performed of patients treated with arch TEVAR (i.e. proximal landing zone 0–3) for various indications between 2007 and 2017. Patients were stratified by the MALAN classification into hostile LAs (i.e. 2/III and 3/III) and favourable LAs (i.e. 0/I–III, 1/I–III, 2/I–II and 3/I–II). Outcome criteria included composite proximal endograft failure (including type Ia endoleak, persistent false lumen perfusion at the level of the most proximal communication between the lumina in aortic dissections, endograft migration and retrograde dissection) and deaths from all causes. Competing risk analyses were performed.

RESULTS: A total of 359 patients (hostile LAs 133; favourable LAs 226) were identified. The median age was 71.0 (62.0–77.0); 78.3% were men. Proximal endograft failure occurred in 28/133 patients (21.1%) in the hostile LA group and in 12/226 (5.3%) in the favourable LA group. On multivariate analysis, hostile LAs were independently associated with proximal endograft failure ($P < 0.0001$). There was no other independent risk factor. Favourable LAs were associated with an increased mortality rate ($P = 0.006$), which could be attributed to the proximal LA subgroup (i.e. 0/I–III and 1/I–III) ($P < 0.0001$), in addition to age ($P < 0.0001$).

CONCLUSIONS: The MALAN classification identifies hostile proximal landing zones for TEVAR, namely 2/III and 3/III LAs, which are associated with dismal proximal endograft performance. The MALAN appears to be an intuitive and valuable tool to improve the preoperative decision-making process.

Keywords: Thoracic aorta endovascular repair • Modified Aortic Landing Areas Nomenclature • Endovascular planning • Thoracic endovascular aortic repair outcome • Proximal endograft failure

ABBREVIATIONS

LA	Landing area
LCCA	Left common carotid artery
MALAN	Modified arch landing areas nomenclature
PLZ	Proximal landing zone
TEVAR	Thoracic endovascular aortic repair

INTRODUCTION

Preoperative planning of thoracic endovascular aortic repair (TEVAR) is primarily based on the identification of a proximal landing zone (PLZ) that allows an adequate procedural feasibility and safety and provides durable effectiveness [1]. This goal implies a healthy aortic wall and an adequate diameter and length (i.e. <40 and ≥ 20 mm, respectively) for endograft deployment [1].

Severe angulation and tortuosity of PLZs also represent well-established determinants of postoperative endograft performance [1–4]. No consensus, however, currently exists on the definition and threshold values of these relevant anatomical features, which, consequently, often remain disregarded. Furthermore, the geometric characteristics of the PLZs determine the distribution and the magnitude of the haemodynamic displacement forces that are exerted on the terminal fixation sites of the endograft after its deployment, which may cause an insufficient proximal seal and/or migration of the endograft [5].

In the aortic arch, PLZs are identified as zone 0–3 according to Ishimaru's map [6], which is based on the requisite of a prophylactic rerouting of the involved supra-aortic vessels, by either extra-anatomical surgical bypass [7] or endovascular procedures [8, 9]. In previous studies, a Modified Arch Landing Areas Nomenclature (MALAN) [10–12] was introduced, which complements Ishimaru's map with the additional use of aortic arch classification in types I, II and III, originally developed for predicting difficult carotid stenting procedures [13]. As a result, in the

MALAN, each landing area (LA) is identified by indicating both the PLZ and the type of arch (e.g. 0/I) (Fig. 1).

Proof of concept analyses showed that the MALAN identifies a consistent geometric and haemodynamic pattern of the aortic arch [10–12] and allows recognition of PLZs with unfavourable biomechanical features for endograft deployment, namely MALAN areas 2/III and 3/III [12].

Notably also, the MALAN has a readily intuitive interpretation because it uses widely shared definitions and is based on viewing the aorta during planning in the parasagittal plane, which is also the plane required intraoperatively for stent graft deployment [10].

The present work was conceived to address the potential value of the MALAN as a predictor of proximal endograft performance, through a *post hoc* application of the MALAN classification to data from a multicentre database of patients treated with TEVAR of the arch.

METHODS

Patient selection

A multicentre retrospective analysis was performed, including 7 European referral centres. Consecutive patients who were treated by TEVAR of the arch, with PLZs 0–3 between 2007 and 2018, regardless of the type of debranching, were reviewed. Indications included aneurysms, dissections, penetrating ulcers/intramural haematomas and traumas. Timing of treatment included elective, urgent and emergency procedures. Exclusion criteria were aortic coarctation; thoraco-abdominal repair; anatomical factors in which the MALAN classification could not be correctly determined, such as anatomical anomalies of the aortic arch (e.g. aberrant right subclavian); bovine arch with landing zone 2 (bovine arch with landing zone 3, was not excluded); previous aortic arch replacement (patients with isolated ascending replacement were not excluded); PLZ sizing performed outside the manufacturers' instructions for use.

The ethics committees at the participating centres approved the study. The need for informed patient consent was waived

	Type I	Type II	Type III
Zone 0			
MALAN	0/I	0/II	0/III
Zone 1			
MALAN	1/I	1/II	1/III
Zone 2			
MALAN	2/I	2/II	2/III
Zone 3			
MALAN	3/I	3/II	3/III

Figure 1: The MALAN, which comprises proximal landing zones according to Ishimaru's aortic arch map and types of arches according to the aortic arch classification (reproduced from ref. [10] with permission from Elsevier Inc.). CCA: common carotid artery; MALAN: Modified Arch Landing Areas Nomenclature.

because of the retrospective nature of the analysis and the use of anonymized data.

Determination of the Modified Arch Landing Areas Nomenclature zone

Preoperative imaging data were used to determine the type of arch [13] for each patient. In detail, the diameter of the left common carotid artery (LCCA) was measured at its origin in the axial view. Multiplanar reconstruction images were used to visualize the origin of the brachiocephalic trunk and the top of the aortic arch in 1 frame. The vertical distance between these 2 locations was used to classify each patient as having a type I, II or III arch. This distance is <1 diameter of the LCCA in a type I arch, between

1 and 2 LCCA diameters in a type II arch and >2 LCCA diameters in a type III arch. Of note, in patients with an aortic aneurysm, if the origin of the LCCA was involved in the arch dilation, the diameter of the right common carotid was used conservatively. In patients with type B dissections, if the extension of the false lumen prevented a clear definition of the top of the arch, the level of the left subclavian artery was considered conservatively as such.

The MALAN LA was determined as previously described [10] by combining the PLZ according to the Ishimaru classification [6] and the type of arch (Fig. 1).

Based on the anatomical and haemodynamic characteristics identified by the MALAN [10–12], patients were stratified as having 'hostile' LAs (i.e. 2/III and 3/III) and 'favourable' LAs (i.e. 0/I–III, 1/I–III, 2/I–II and 3/I–II). A further stratification identified a

proximal favourable LAs subgroup (i.e. 0/I–III and 1/I–III) and a distal favourable LAs subgroup (i.e. 2/I–II and 3/I–II).

Outcome criteria

The primary outcome end point was proximal endograft failure, which was defined as a composite index including the development of any or all of the following complications: type Ia endoleak [14]; persistent false lumen perfusion at the level of the most proximal communication between the lumina in aortic dissections; endograft migration, defined as a change of movement in excess of 10 mm from proximal aortic landmarks to the proximal stent tip and the proximal stent circumferential appearance [14]; and retrograde aortic dissection. The second outcome end point was all-cause deaths. Data on cause-specific deaths could not be adequately retrieved from the databases.

Postoperative care and follow-up schedules differed per institution but were in accordance with TEVAR guidelines [1]. Accordingly, at least immediate and 1-year postoperative computed tomographic scans were performed, with yearly follow-up thereafter.

Statistical methods

The mean (standard deviation) for normal variables or the median (range) for non-normal variables was used to describe continuous parameters, whereas counts and % were used for categorical variables.

The hostile LA and favourable LA subgroups were compared using the χ^2 test or the Fisher's exact test when appropriate. The Shapiro–Wilk test demonstrated the non-normal distribution of continuous variables. Hence, a non-parametric test (i.e. Kruskal–Wallis test) was used, despite the large sample size.

The follow-up median time was determined by the Kaplan–Meier estimate of potential follow-up, where survival was defined as the event.

Time to complication was defined as the time from TEVAR to the onset of the first complication included in the definition of the composite proximal endograft failure; time to death was defined as the time from TEVAR to death. Patients without adverse events at the last follow-up were entered in the survival analysis as censored.

Proximal endograft failure and death were defined as 2 failure competing risk events. Competing risk analyses were used to describe proximal endograft failure and all-cause death for the hostile and favourable LA groups. Differences among the patient subgroups were tested with Gray's test.

Patients were categorized by type of endograft (CTAG/TAG, W. L. Gore & Associates, Flagstaff, AZ, USA; Zenith, Cook Inc., Bloomington, IN, USA; Valiant and Talent, Medtronic, Santa Rosa, CA, USA; Relay, Terumo Aortic, Bolton Medical Inc., Sunrise, FL, USA and others), by surgical timing (elective, urgent, emergency) and by indication to treatment (aneurysm, acute dissection, intramural haematomas/penetrating aortic ulcer and traumatic aortic injury, chronic dissection with aneurysm). We also considered age [15], gender [16], hypertension, chronic kidney disease [17], maximum aortic diameter [18], type of endograft, surgical timing, indication of treatment and maximum proximal diameter of the endograft [18] as potential confounders. A proportional hazards model for the subdistribution of a competing risk was used to

define the hazard of proximal endograft failure and death for hostile LAs versus favourable LAs.

All tests were 2-sided and considered statistically significant at the 0.05 level. Statistical analyses were done with SAS software, version 9.4 (SAS Institute, Inc., Cary, NC, USA).

RESULTS

Baseline and procedural characteristics

A total of 359 patients were retrieved. The hostile LA group included 133 cases, and the favourable LA group included 226 cases. The proximal favourable LA subgroup listed 48 cases and the distal favourable LA, 178 cases.

Patient demographics and medical history are reported in [Supplementary Material, Table S1](#); aortic characteristics and procedural details are reported in Table 1.

The median age was 71.0 (range 62.0–77.0) years; 78.3% were men. There was no difference between the groups in terms of age ($P=0.10$), whereas the hostile LA group had fewer men ($P=0.02$). Patients with hostile LA more frequently had hypertension ($P=0.01$), hyperlipidaemia ($P=0.03$) and chronic kidney disease ($P=0.01$).

The 2 groups had similar indications for treatment ($P=0.13$) except for traumatic aortic injury, which was less common in the hostile LA group (6.8% vs 16.0%; $P=0.01$). The hostile LA group also had a greater maximum aortic diameter (60.0 vs 54.0 mm; $P=0.002$) and a larger proximal endograft diameter (37.0 vs 36.0 mm; $P=0.004$).

Clinical outcome

The median follow-up duration was 37.4 months (95% confidence interval 28.6–42.0 months). The estimated overall survival rate after 5 years was $71.8 \pm 2.8\%$ (% of survival \pm standard error) (patients at risk: $n=63$).

Complications identifying a proximal endograft failure occurred in 28/133 (21.1%) patients of the hostile LA group (i.e. 14 cases in LA 3/III and 14 cases in LA 2/III), and in 12/226 (5.3%) of the favourable LA group. In the proximal favourable LA subgroup, complications occurred in 2/48 (4.2%) (i.e. 2 cases in 1/III) and in the distal favourable LA subgroup, they occurred in 10/178 (5.6%) (i.e. 4 in 2/I, 3 in 2/II, 1 in 3/I and 2 in 3/II). In detail, composite proximal endograft failure included type Ia endoleak in 25 cases, associated with endograft migration in 1 case and type Ib endoleak in 1 case; endograft migration in 7 cases (in 1 with type Ia endoleak); retrograde aortic dissection in 2 cases; and persistent false lumen perfusion at the level of the most proximal communication between lumina in 6 cases.

Other complications not related to proximal endograft performance were type Ib endoleak in 7 cases (in 1 with type Ia endoleak); type II endoleak in 3 cases; type III endoleak in 3 cases; endotension in 1 case; and stent graft infection, aorto-oesophageal fistula, distal stent graft-induced new entry tear, paraplegia, stent graft thrombosis and stent graft collapse in 1 case, respectively.

There were 90 deaths: 65 in the favourable LA group and 25 in the hostile LA group.

Table 1: Aortic characteristics and procedural details

	Hostile LAs (n = 133)	Favourable LAs (n = 226)	P-value
Indication for treatment, n (%)			0.13
Aneurysm	69 (51.9)	113 (50.2)	
Acute dissection	21 (15.8)	30 (13.3)	
IMH/PAU	21 (15.8)	30 (13.3)	
Traumatic aortic injury	9 (6.8)	36 (16.0)	
Chronic dissection with aneurysm	13 (9.8)	16 (7.1)	
Timing, n (%)			0.32
Elective	89 (66.9)	137 (61.2)	
Urgent	23 (17.3)	37 (16.5)	
Emergency	21 (15.8)	50 (22.3)	
ASA classification, n (%)			0.52
I		1 (0.5)	
II	8 (8.0)	9 (4.7)	
III	52 (52.0)	108 (56.5)	
IV	21 (21.0)	46 (24.1)	
V	19 (19.0)	27 (14.1)	
Stent graft type, n (%)			0.07
Medtronic Valiant ^a	59 (44.4)	84 (37.3)	
Gore CTAG ^b	49 (36.8)	112 (49.8)	
Bolton Relay and others	11 (8.3)	9 (4.0)	
Cook Zenith	14 (10.5)	20 (8.9)	
Maximum aortic diameter (mm), median (range)	60.0 (50.0–67.5)	54.0 (40.0–65.0)	0.002
Proximal stent graft diameter (mm), median (range)	37.0 (34.0–40.0)	36.0 (32.0–40.0)	0.004
Oversizing (%), median (range)	14.2 (10.8–21.4)	15.6 (11.1–20.5)	0.55
Debranching, n (%)			0.02
Surgical	32 (28.8)	79 (35.4)	
Chimney	2 (1.5)	10 (4.5)	
Any other adjunctive procedures, n (%)	28 (25.7)	60 (32.1)	0.25

^aIncludes 3 patients treated with Medtronic Talent stent graft.

^bIncludes 21 patients treated with Gore TAG stent graft.

ASA: American Society of Anesthesiologists; IMH: intramural haematoma; LA: landing area; PAU: penetrating aortic ulcer. Values in boldface indicate statistical significance.

Outcome analysis

Univariate competing risk analysis showed that hostile LAs were significantly associated with an increased risk of proximal endograft failure ($P < 0.0001$) (Fig. 2). This was also the case when proximal and distal favourable LA subgroups were considered separately ($P < 0.0001$) (Fig. 3).

On multivariate competing risk analysis (Table 2), hostile LAs remained independently associated with proximal endograft failure [subdistribution hazard ratio 5.45 (2.59–11.45); $P < 0.0001$]. The model did not identify any other independent risk factor.

Regarding the risk of all-cause death, univariate competing risk analysis showed that the favourable LA group had a higher risk of death ($P = 0.0325$) (Fig. 4). When proximal and distal favourable LA subgroups were considered separately (Fig. 5), however, it appeared that the greatest risk of death was attributed to the proximal favourable LA subgroup only ($P < 0.0001$) and that there was no difference between hostile LAs and distal favourable LAs ($P = 0.20$). Cumulative curves are reported in [Supplementary Material, Figs S1 and S2](#).

On multivariate competing risk analysis (Table 3), favourable LAs remained independently associated with an increased risk of death at follow-up [hostile versus favourable, subdistribution hazard ratio 0.46 (0.26–0.80); $P = 0.006$]. In addition, age was independently associated with an increased all-cause mortality rate [subdistribution hazard 1.06 (1.03–1.09); $P < 0.0001$].

DISCUSSION

Previous outcome analyses showed that, whereas TEVAR of the descending aorta provides remarkable long-term clinical success rates [19], endovascular repair of aortic arch disease remains associated with much less satisfactory results [20]. The introduction of new devices specifically designed to conform with the geometry of the arch have undeniably improved the performance of the endografts [21, 22]. Concerns persist, however, regarding the durability of endovascular treatment due to the continuous aortic remodelling induced by the endograft [22, 23], which is related to its biomechanical interaction with the aortic arch wall, particularly in zones 2 and 3 [12, 22, 24].

The present work provides evidence that the PLZs identified by the MALAN as geometrically and haemodynamically hostile for endograft deployment (i.e. 2/III and 3/III) due to the presence of consistent suboptimal angulation and tortuosity and high displacement forces [10–12] are independently associated with dismal proximal endograft performance after TEVAR. Hence, this newly introduced nomenclature appears to be a valuable tool to improve the preoperative decision-making process.

In this respect, the onset of complications after TEVAR of the arch indicates that following the patient-specific preoperative planning, which is currently based on static imaging protocols only [11], does not *per se* guarantee clinical success.

The MALAN relies on biomechanical modelling of anatomical patterns of the aortic arch and introduces in a systematic and

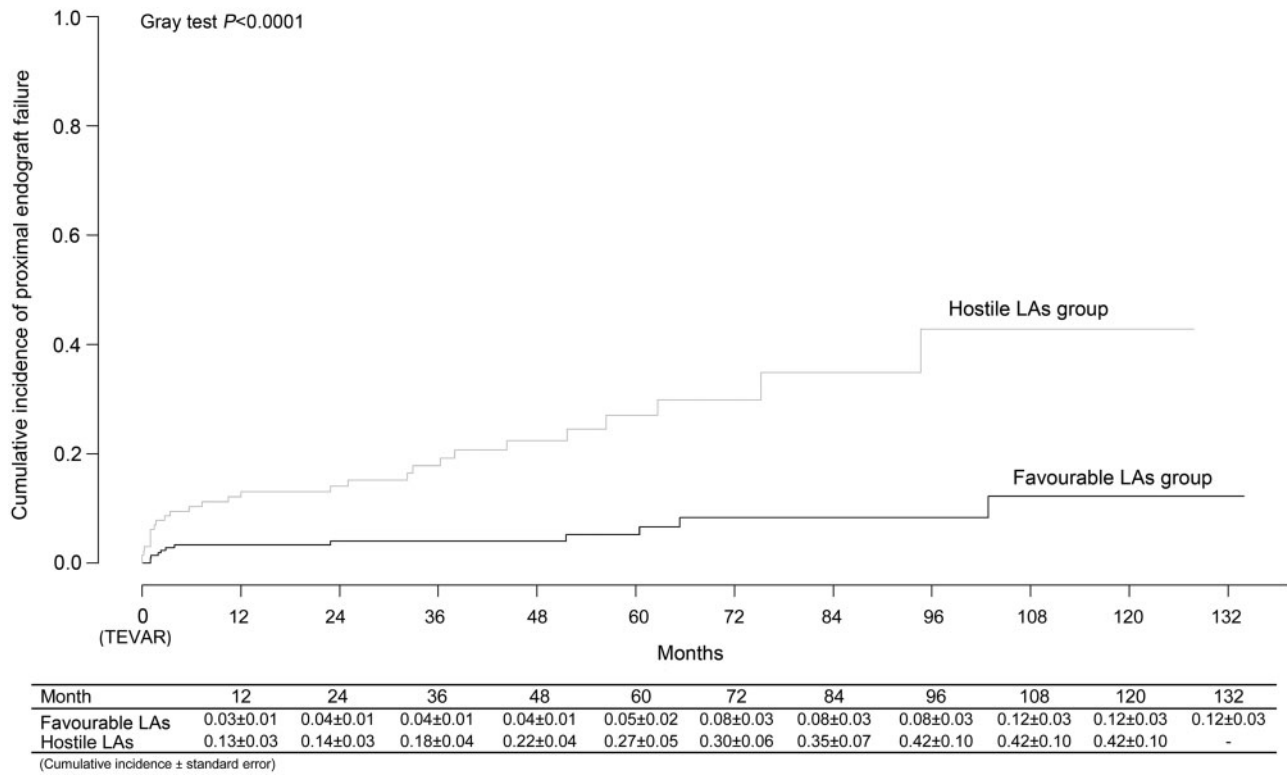


Figure 2: Estimated competing risk curves for the probability of proximal endograft failure in hostile and favourable LA groups. LA: landing area; TEVAR: thoracic endovascular aortic repair.

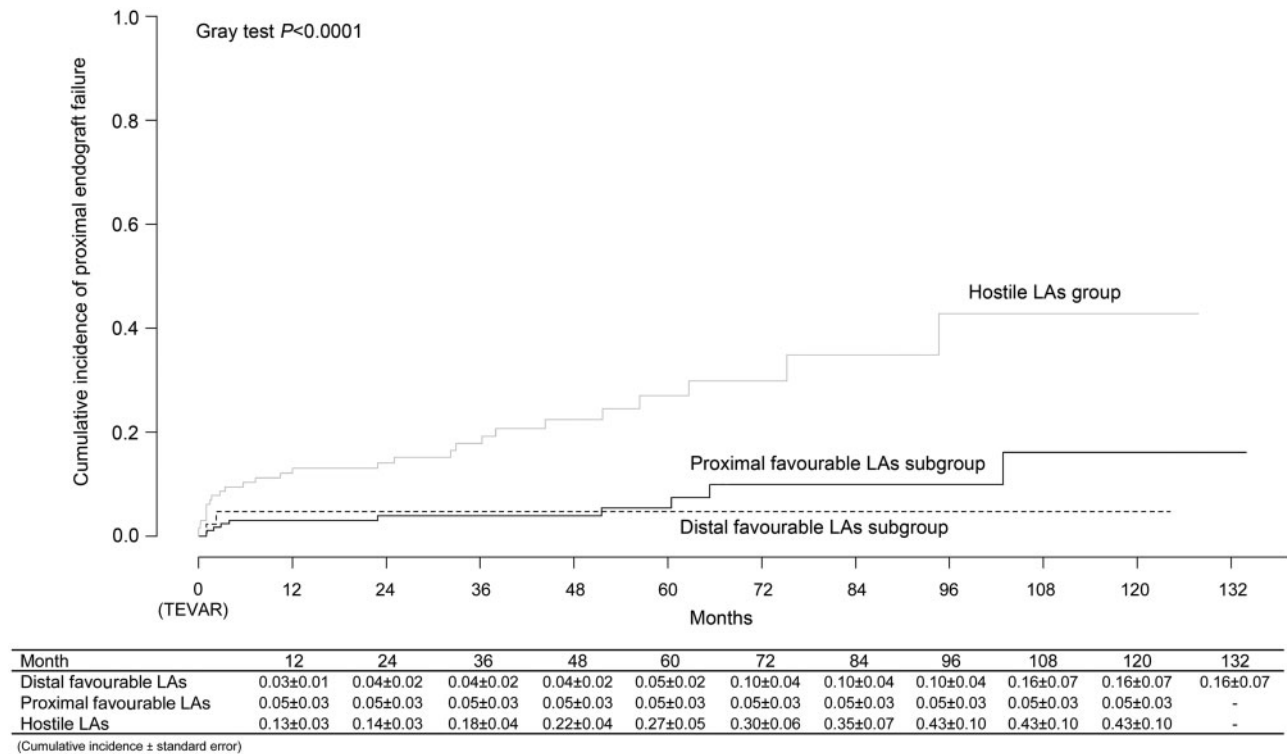


Figure 3: Estimated competing risk curves for the probability of proximal endograft failure in hostile LA group and proximal favourable and distal favourable LA subgroups. LA: landing area; TEVAR: thoracic endovascular aortic repair.

Table 2: Multivariate cumulative incidence analysis of risk factors for proximal endograft failure

	Subdistribution hazard ratio	P-value
MALAN group		<0.0001
Hostile	5.45 (2.59–11.45)	
Favourable	Ref	
Stent graft type		0.76
Gore CTAG/TAG	0.68 (0.29–1.57)	
Bolton Relay and others	1.02 (0.19–5.41)	
Cook Zenith	1.12 (0.38–3.33)	
Medtronic Valiant/Talent	Ref	
Timing		0.08
Urgent	0.17 (0.04–0.80)	
Emergency	0.68 (0.16–2.89)	
Elective	Ref	
Indication		0.20
Acute dissection	1.61 (0.42–6.18)	
PAU/trauma	0.42 (0.11–1.60)	
Aneurysm/chronic dissection	Ref	
Proximal stent graft diameter	1.08 (0.99–1.17)	0.10
Age	1.00 (0.95–1.04)	0.85
Gender		0.96
Male	1.02 (0.42–2.52)	
Female	Ref	
Hypertension	1.56 (0.53–4.62)	0.43
Chronic kidney disease	0.94 (0.35–2.50)	0.89
Maximum aortic diameter	0.99 (0.95–1.02)	0.37

MALAN: Modified Arch Landing Areas Nomenclature; PAU: penetrating aortic ulcer.

Values in boldface indicate statistical significance.

reproducible fashion dynamic measurements with an apparent predictive value regarding proximal endograft performance. From a clinical standpoint, our observations imply that during preoperative assessment, despite the fact that a given landing zone is deemed adequate based on patient-specific planning, a different, namely, a more proximally located landing zone, may be considered to obtain better clinical results, even though such a choice poses the issue of a more complex and technically demanding debranching of the involved supra-aortic vessels. The use of scalloped devices may represent a viable option to resolve this matter [25, 26], but further specific studies are necessary to prove the case.

Further studies are also required to address how the different endovascular debranching techniques deal with the anatomical and dynamic features described by the MALAN. In this respect, the take-off angles of the supra-aortic branches, which predict a difficult cannulation according to the original description of the types of arches [13], may expose the chimneys or the bridging stents to increased mechanical stress, which may affect the sealing [10].

When we considered the risk of all-cause mortality, our data showed that, counterintuitively, the MALAN favourable LAs are associated with an increased risk of death. In fact, only the proximal favourable LA subgroup, which includes all zones 0 and 1, is associated with a greater mortality rate (Fig. 5). This finding appears related to the magnitude of the debranching procedure required in more proximally located landing zones and reflects the severity of aortic disease in these patients.

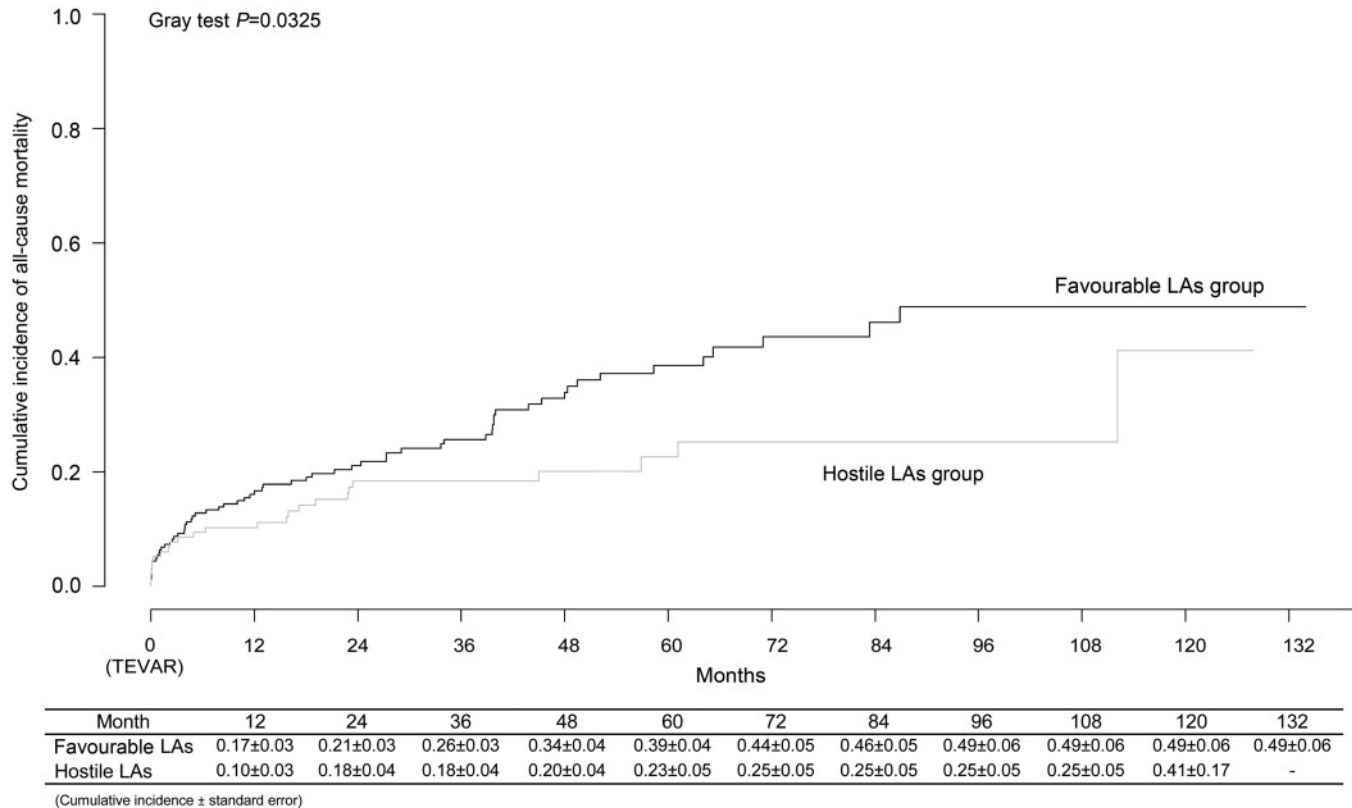
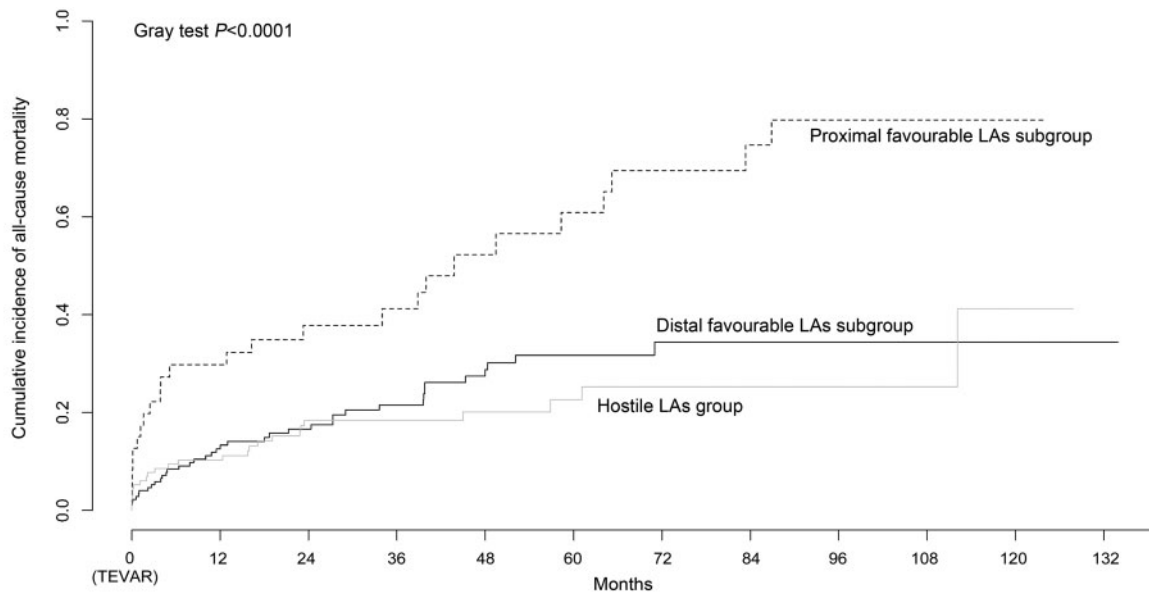


Figure 4: Estimated competing risk curves for the probability of all-cause deaths in hostile and favourable LA groups. LA: landing area; TEVAR: thoracic endovascular aortic repair.



Month	12	24	36	48	60	72	84	96	108	120	132
Distal favourable LAs	0.13±0.03	0.17±0.03	0.22±0.04	0.29±0.04	0.32±0.05	0.34±0.05	0.34±0.05	0.34±0.05	0.34±0.05	0.34±0.05	0.34±0.05
Proximal favourable LAs	0.30±0.07	0.38±0.08	0.41±0.08	0.52±0.08	0.61±0.09	0.69±0.09	0.75±0.09	0.80±0.09	0.80±0.09	0.80±0.09	-
Hostile LAs	0.10±0.03	0.18±0.04	0.18±0.04	0.20±0.04	0.23±0.05	0.25±0.05	0.25±0.05	0.25±0.05	0.25±0.05	0.41±0.17	-

(Cumulative incidence ± standard error)

Figure 5: Estimated competing risk curves for the probability of all-cause mortality in the hostile LA group and the proximal and distal favourable LA subgroups. LA: landing area; TEVAR: thoracic endovascular aortic repair.

Table 3: Multivariate cumulative incidence analysis of risk factors for all-cause mortality

	Subdistribution hazard ratio	P-value
MALAN group		0.006
Hostile	0.46 (0.26–0.80)	
Favourable	Ref	
Stent graft type		0.84
Gore CTAG/TAG	1.09 (0.67–1.79)	
Bolton Relay and others	1.14 (0.45–2.88)	
Cook Zenith	0.72 (0.28–1.85)	
Medtronic Valiant/Talent	Ref	
Timing		0.54
Urgent	1.60 (0.69–3.68)	
Emergency	1.01 (0.51–1.98)	
Elective	Ref	
Indication		0.77
Acute dissection	0.67 (0.23–1.96)	
PAU/trauma	0.89 (0.37–2.12)	
Aneurysm/chronic dissection	Ref	
Proximal stent graft diameter	1.02 (0.96–1.08)	0.58
Age	1.06 (1.03–1.09)	<0.0001
Gender		0.48
Male	0.81 (0.46–1.44)	
Female	Ref	
Hypertension	0.71 (0.38–1.31)	0.27
Chronic kidney disease	1.38 (0.69–2.75)	0.37
Maximum aortic diameter	1.01 (0.99–1.02)	0.14

MALAN: Modified Arch Landing Areas Nomenclature; PAU: penetrating aortic ulcer.

Values in boldface indicate statistical significance.

Age, as expected, was an independent determinant of death, whereas we failed to confirm the association between reduced survival rates and chronic kidney disease [17], likely due to the use of creatinine, which is recognized as an insensitive marker of renal function.

Finally, the MALAN studies [10–12], including the present one, provide a clinical model to implement current instructions for use of commercially available endografts, to develop new devices with specific technical designs and to compare in a clinical setting the conformability of the different endografts presently available [21].

Limitations

We recognize some limitations of our study, including the baseline differences between the study groups and those inherent in its retrospective fashion, especially the median follow-up duration of 3 years over a study period of 10 years. Also, differences in clinical practices among the participating centres may be seen as a potential source of bias, as can the inclusion of different indications for TEVAR. On the other hand, these factors may improve the generalizability of the study findings.

CONCLUSION

This work proves in a large cohort of patients the predictive value of the MALAN classification to identify hostile PLZs for TEVAR, which are associated with sobering clinical outcomes related to proximal endograft performance. The MALAN appears to be a practical method to improve the TEVAR preoperative decision-making process and potentially to implement stent graft design.

SUPPLEMENTARY MATERIAL

Supplementary material is available at EJCTS online.

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Author contributions

Massimiliano M. Marrocco-Trischitta: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Writing—original draft; Writing—review & editing. **Hector W. de Beaufort:** Conceptualization; Data curation; Formal analysis; Writing—original draft. **Gabriele Piffaretti:** Data curation; Formal analysis; Investigation; Writing—review & editing. **Stefano Bonardelli:** Conceptualization; Data curation; Formal analysis; Writing—review & editing. **Mauro Gargiulo:** Conceptualization; Data curation; Formal analysis; Writing—review & editing. **Michele Antonello:** Conceptualization; Data curation; Formal analysis; Writing—review & editing. **Joost A. van Herwaarden:** Conceptualization; Data curation; Formal analysis; Writing—review & editing. **Sara Boveri:** Data curation; Formal analysis; Methodology; Writing—original draft. **Raffaello Bellosta:** Conceptualization; Data curation; Formal analysis; Writing—review & editing. **Santi Trimarchi:** Conceptualization; Data curation; Formal analysis; Funding acquisition; Writing—review & editing.

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