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Outcome of Single *Versus* Dual Antiplatelet Therapy After Complex Endovascular Aortic Repair

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ABSTRACT

Introduction: Despite the widespread use of branched (bEVAR) and fenestrated endovascular aortic repair (fEVAR) for complex aortic pathologies, there are no reliable recommendations regarding postsurgery antiplatelet therapy. We therefore evaluated the outcome of single (SAPT) and dual antiplatelet therapy (DAPT) following fEVAR and bEVAR.

Methods: A total of 63 patients from two German centers treated for complex aortic pathologies were included in this retrospective study. Patient data and computed tomography angiograms were analyzed. Kaplan–Meier analyses for overall survival and freedom from target vessel (TV)-related complications were performed. The outcomes were compared between SAPT *versus* DAPT and bEVAR *versus* fEVAR. Univariate logistic regression was applied to analyze the correlation between TV patency and various anatomical aortic parameters.

Results: In total, 30 patients were treated with fEVAR and 33 with bEVAR. Of these, 19 patients received SAPT and 44 received DAPT postsurgery. Anatomical aortic characteristics and comorbidities were comparable among groups. Overall survival was 95% (±5.1) for SAPT and 88% (±8.8) for DAPT after 36 mo of follow-up. Patency was evaluated individually for each TV SAPT *versus* DAPT (celiac trunk 100% ± 0 *versus* 87% ± 9.6; superior mesenteric artery 86% ± 13.2 *versus* 100% ± 0; left renal artery 92% ± 8.0 *versus* 95% ± 3.6; right renal artery 72% ± 15.2 *versus* 81% ± 9.9). Freedom from endoleak was 35% (±13.7) for SAPT *versus* 30% (±13.8) for DAPT. There was no statistically significant difference for SAPT *versus* DAPT or for bEVAR *versus* fEVAR. Further, none of the anatomical aortic characteristics and bridging stent graft-related parameters analyzed predicted TV occlusion in logistic regression analysis.

Conclusions: We did not observe differences in overall survival, endoleak, and TV patency rates between SAPT and DAPT treated patients following bEVAR and/or fEVAR. Patient-

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specific factors therefore appear to be more relevant for the long-term outcomes rather than the antiplatelet regime applied postsurgery.

Introduction

Branched (bEVAR) and fenestrated endovascular aortic repair (fEVAR) have become viable treatment options for complex aortic pathologies affecting the reno-visceral aortic segment, such as thoraco-abdominal aortic aneurysm (TAAA), penetrating aortic ulcer, and type B aortic dissection.[1-6] While devices are constantly evolving and surgeons gain more experience in their use throughout institutions, there is still a considerable risk for complications during the follow-up (FU).[7-11]

Yet, studies investigating potential contributors of long-term complications are rather sparse. Some technical aspects of bEVAR and/or fEVAR procedures, such as the length of the target vessel (TV) landing zone, the number of TVs treated within the procedure, and total aortic coverage, have been identified to be associated with TV occlusion and/or endoleak (EL) rates.[9,12] However, less attention has been paid to the effects of different anticoagulative or antiplatelet regimens following f/bEVAR. While some studies suggest that patients receiving anticoagulation post fEVAR and/or bEVAR are at higher risk of developing persistent type II EL (TIIEL), others report no effect regarding that endpoint.[13,14] Even fewer studies are currently available that evaluated the relevance of antiplatelet therapy for postsurgical complication rates, although enhanced platelet activation has been described in patients with abdominal aortic aneurysm pre- and post-EVAR.[15,16]

The lack of available data leaves it to the surgeon's experience and preference, which antiplatelet regimen to choose following complex endovascular aortic procedures. A recent study suggests that the number of patients discharged on dual (DAPT) *versus* single antiplatelet (SAPT) therapy regimes has increased throughout the past years.[17] However, it is unclear how SAPT *versus* DAPT therapy affects the outcome and complication rates at long-term.

The present retrospective study evaluates the outcome and complication rates of SAPT *versus* DAPT following fEVAR and bEVAR for patients with complex aortic pathologies.

Methods

Data collection and FU

In this retrospective study, we collected clinical data from patients undergoing fEVAR or bEVAR at the University Hospital Düsseldorf, Germany and the University Hospital Münster, Germany between January 1, 2012, and June 31, 2019, and June 6, 2018, and March 2, 2020 respectively. All relevant data were retrieved from archived medical records for subsequent analysis. FU data were collected if available. Primary outcomes were patient survival, EL, and TV patency. TAAA was classified according to the Crawford classification.[18]

Technical success was defined as successful endovascular implantation of the stent graft with preservation of antegrade flow to the TVs and the absence of type I or III EL at the final periprocedural angiogram.

Patients were distributed according to their postprocedural antiplatelet therapy regime, which consisted of either acetylsalicylic acid (ASS) monotherapy (SAPT) or additional Clopidogrel or Ticagrelor for at least 6 wk (DAPT). Patients receiving anticoagulation postsurgery were excluded from the study to focus only on the effects of antiplatelet therapy on the aforementioned endpoints. Postprocedural complications were defined as follows: major bleeding: peri or postprocedural transfusion or resurgery for acute bleeding event; infection: documented postprocedural sepsis needing intravenous antibiotics; cardiovascular: myocardial infarction, congestive heart failure, and arrhythmia; neurologic: transitory ischemic attack, stroke, and paraplegia; Nephrological: documented acute kidney failure and kidney infarction; pulmonary: respiratory insufficiency, pulmonary embolism, and pneumonia; delayed wound healing: access site wound revision required; stent migration: documented stent migration in FU computed tomography (CT) scan; and stent material failure: documented graft failure in FU CT scan.

CT-angiography data collection

Pre- and postprocedure CT angiography (CTA) scans were analyzed in multiplanar reconstruction using Horos (horosproject.org, v4.0.0 RC5). Preimplantation CTA scans were analyzed for anatomical TV- and aneurysm-related parameters. Postimplantation CTA scans were used to define proximal and distal landing zones according to the generally accepted reporting standards.[19] Based on the measurements taken from CTA scans and available procedural data, the oversize index for TV bridging stent grafts was calculated as bridging stent graft diameter divided by the TV diameter.

Statistical analysis

Categorical variables are presented as relative frequencies with percentages; continuous variables are shown as mean and standard deviation. Shapiro–Wilk test was used for assessment of normality distribution. Chi^2 test was applied for categorical variables and in cases of $n < 5$, Fisher's exact test was applied. For continuous variables, Student's *t*-test or Mann-Whitney-*U* test were applied. A P value of < 0.05 was considered statistically significant. For statistical analysis, SPSS (V.25 SPSS Inc, Chicago, USA) was used. All graphs were created using GraphPad Prism (V.10.1 GraphPad Software, Inc., San Diego, USA), which was also used for Kaplan–Meier curves and respective log-rank tests.

Ethical approval

The study was approved by the local ethics committees at Heinrich Heine University Düsseldorf, Germany, and University Münster, Germany (approval IDs 2019-544 and 2019-720-b-S) and followed all applying standards for good scientific practice and the Declaration of Helsinki. Due to the sole retrospective character of the study, no patient consent had to be obtained, as consented by both local ethics committees.

Results

Patient and aortic characteristics

A total of 63 patients were included in this study of which 30 were treated with fEVAR and 33 with bEVAR (Fig. 1A). Technical success was achieved in all cases. Patients were subdivided into two groups, depending on whether they were discharged on a SAPT or DAPT postsurgery regime. 10 patients received SAPT following fEVAR, and 9 patients following bEVAR, while the overall majority of patients received DAPT postsurgery ($n = 20$ for fEVAR and $n = 24$ for bEVAR, Fig. 1B). The mean age of the cohort was 70.1 y in the overall cohort with 47 males (74.6%) and 16 females (25.4%). The distribution of relevant comorbidities and body mass index did not differ significantly between groups (Table 1). Prior to surgery, 48 patients (76.2%) were on SAPT, and there were no significant intergroup differences regarding use of statins or antihypertensive drugs (Table 2). The majority of patients in the DAPT group received ASS and additional Clopidogrel for 6 mo ($n = 20$, 45.5%) or lifelong ($n = 13$, 29.5%, Fig. 1C).

Most patients underwent endovascular repair for TAAA. In detail, there were 15 patients (23.8%) with type II TAAA and 32 patients (50.8%) with type IV TAAA. Of note, approximately one fifth of all patients were treated in an emergency or urgent setting with 9 (14.3%) symptomatic and 4 (6.3%) ruptured cases. Medium maximum aortic diameter across the pathologies was 60.9 mm, and there were no significant intergroup differences regarding other pathology-specific parameters (Table 3).

TV configuration

Following multiplanar reconstruction of presurgery CTA scans, we compared the anatomic configuration of the visceral and renal TV, therefore celiac trunk, the superior mesenteric artery (SMA), the left (LRA) and right renal artery (RRA). Here, we did not observe significant differences in offspring angles across all subgroups except for the LRA in the coronary plane. Here, DAPT bEVAR patients showed more open angles in the coronary plane *versus* SAPT bEVAR (97.8° *versus* 109°, $P = 0.013$). Considering TV diameters, the maximum SMA diameter was significantly larger in the SAPT when compared to the DAPT group (7.44 mm *versus* 6.9 mm, $P = 0.047$). Other than that, no significant differences were observed when comparing TV-related parameters between the bEVAR *versus* fEVAR subgroups (Supplementary Table 1).

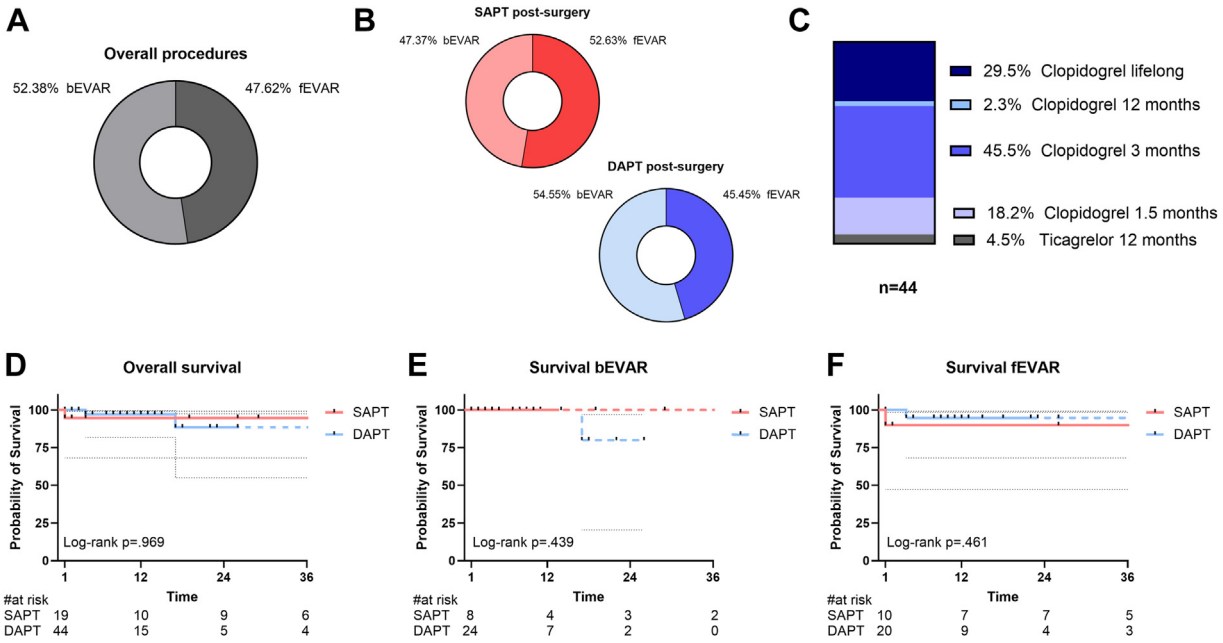

Fig. 1 – Procedure distribution and postprocedural medication and survival. Overall distribution of endovascular procedures in the study population (A). Distribution of postsurgery antiplatelet therapy after respective endovascular therapy for SAPT) and DAPT (B). Distribution of DAPT postsurgery drug regime in addition to acetylsalicylic acid (C). Overall survival assessed by Kaplan–Meier method comparing overall SAPT *versus* DAPT (D) and survival in bEVAR (E) and fEVAR (F) patients separately. Data are shown as percentage (A-C) or Kaplan–Meier estimates displayed with 95% CI, time is in months (D-F). *P* value of log-rank test is displayed in the graph. bEVAR = branched endovascular aortic repair; fEVAR = fenestrated endovascular aortic repair; SAPT = single antiplatelet therapy; DAPT = dual antiplatelet therapy; # = number.

Table 1 – Patient demographics and comorbidities.

Patient characteristics	Total cohort	SAPT			DAPT			*P* value		
	($n = 63$)	Overall ($n = 19$)	fEVAR ($n = 10$)	bEVAR ($n = 9$)	Overall ($n = 44$)	fEVAR ($n = 20$)	bEVAR ($n = 24$)	SAPT *versus* DAPT	SAPT fEVAR *versus* DAPT fEVAR	SAPT bEVAR *versus* DAPT bEVAR
Age (years)	70.1 ± 7.19	68.58 ± 7	69 ± 8.64	68.11 ± 5.1	70.75 ± 7.25	72.45 ± 5.81	69.33 ± 8.11	0.333	0.376	0.887
Male gender	47 (74.6%)	13 (68.4%)	8 (80%)	5 (55.6%)	34 (77.3%)	18 (90%)	16 (66.7%)	0.459	0.448	0.555
Comorbidities										
ASA score ≥ 3	49 (77.8%)	13 (68.4%)	7 (70%)	6 (66.7%)	36 (81.8%)	17 (85%)	19 (79.2%)	0.240	0.333	0.456
Hyperlipidemia	25 (39.7%)	10 (52.6%)	5 (50%)	5 (55.6%)	15 (34.1%)	8 (40%)	7 (29.2%)	0.167	0.602	0.160
Hypertension	60 (95.2%)	18 (94.7%)	9 (90%)	9 (100%)	42 (95.5%)	19 (95%)	23 (95.8%)	0.902	0.605	0.534
History of MI	11 (17.5%)	4 (21.1%)	2 (20%)	2 (22.2%)	7 (15.9%)	6 (30%)	1 (4.2%)	0.622	0.559	0.108
VHD	3 (4.8%)	0	0	0	3 (6.8%)	2 (10%)	1 (4.2%)	0.243	0.301	0.534
Arrhythmia	9 (14.3%)	3 (15.8%)	1 (10%)	2 (22.2%)	6 (13.6%)	5 (25%)	1 (4.2%)	0.823	0.333	0.108
CAD	17 (27%)	5 (26.3%)	3 (30%)	2 (22.2%)	14 (31.8%)	9 (45%)	5 (20.8%)	0.629	0.522	0.931
PAD	19 (30.2%)	5 (26.3%)	3 (30%)	2 (22.2%)	14 (31.8%)	5 (25%)	9 (37.5%)	0.460	0.238	0.499
DMTII	6 (9.5%)	1 (5.3%)	1 (10%)	0	5 (11.4%)	2 (10%)	3 (12.5%)	0.449	0.999	0.266
CRF	12 (19%)	4 (21.1%)	2 (20%)	2 (22.2%)	8 (18.2%)	5 (25%)	3 (12.5%)	0.790	0.760	0.488
COPD	16 (25.4%)	4 (21.1%)	1 (10%)	3 (33.3%)	12 (27.3%)	6 (30%)	6 (25%)	0.680	0.271	0.632
History of smoking	35 (55.6%)	11 (57.9%)	5 (50%)	6 (66.7%)	24 (54.5%)	11 (55%)	13 (54.2%)	0.806	0.796	0.518
History of cancer	13 (20.6%)	4 (21.1%)	2 (20%)	2 (22.2%)	9 (20.5%)	5 (25%)	4 (16.7%)	0.957	0.760	0.712
BMI	**80.0 (69.0-95.0)**	**26.18 (22.74-29.66)**	**26.5 (22.74-30.85)**	**25.37 (21.19-29.77)**	**27.46 (23.77-29.34)**	**27.12 (24.9-29.66)**	**26.83 (22.72-29.34)**	0.716	0.792	0.684
	($n = 61$)	($n = 18$)	($n = 10$)	($n = 8$)	($n = 43$)	($n = 20$)	($n = 23$)			
Normal weight	21 (34.3%)	7 (38.9%)	4 (40%)	3 (37.5%)	14 (32.6%)	5 (25%)	9 (39.1%)	0.635	0.398	0.935
Overweight	26 (42.6%)	6 (33.3%)	4 (40%)	2 (25%)	20 (46.5%)	11 (55%)	9 (39.1%)	0.343	0.439	0.472
Obesity	8 (13.1%)	1 (5.3%)	0	1 (12.5%)	7 (16.3%)	4 (20%)	3 (13%)	0.258	0.129	0.968
Extreme obesity	5 (8.2%)	3 (15.8%)	2 (20%)	1 (12.5%)	2 (4.7%)	0	2 (8.7%)	0.119	0.038	0.754

Data are presented as absolute frequencies (percentages) or mean ± standard deviation (SD) as indicated as roman or median and quartiles (Q1+3) for non-normally distributed continuous data as indicated as bold. The *P* values are presented for all procedures SAPT *versus* DAPT and SAPT *versus* DAPT fEVAR and bEVAR patients separately, applying Student's *t*-test, Mann-Whitney-*U*, or chi^2 test where applicable.

ASA = American Society of Anesthesiologists; MI = myocardial infarction; VHD = valvular heart disease; CAD = coronary artery disease; PAD = peripheral artery disease; DMTII = Diabetes mellitus Type II; CRF = chronic renal failure; COPD = chronic obstructive pulmonary disease; BMI = body mass index; SAPT = single antiplatelet therapy; DAPT = dual antiplatelet therapy; fEVAR = fenestrated endovascular aortic repair; bEVAR = branched endovascular aortic repair.

Table 2 – Patient medication prior to surgery.

Patient medication	Total cohort	SAPT			DAPT			P value		
Prior to surgery	($n = 63$)	Overall ($n = 19$)	fEVAR ($n = 10$)	bEVAR ($n = 9$)	Overall ($n = 44$)	fEVAR ($n = 20$)	bEVAR ($n = 24$)	SAPT *versus* DAPT	SAPT fEVAR *versus* DAPT fEVAR	SAPT bEVAR *versus* DAPT bEVAR
Statins	46 (73%)	10 (52.6%)	5 (50%)	5 (55.6%)	36 (81.8%)	18 (90%)	18 (75%)	0.017	0.015	0.279
ACE inhibitors	30 (47.6%)	10 (52.6%)	6 (60%)	4 (44.4%)	20 (45.5%)	12 (60%)	8 (33.3%)	0.601	0.999	0.555
CCB	19 (30.2%)	5 (26.3%)	2 (20%)	3 (33.3%)	14 (31.8%)	9 (45%)	5 (20.8%)	0.662	0.180	0.456
AT1-inhibitors	17 (27%)	4 (21.1%)	1 (10%)	3 (33.3%)	13 (29.5%)	5 (25%)	8 (33.3%)	0.486	0.333	0.999
ß-blocker	42 (66.7%)	14 (73.7%)	7 (70%)	7 (77.8%)	28 (63.6%)	15 (75%)	13 (54.2%)	0.437	0.770	0.216
Anticoagulants	2 (3.2%)	0	0	0	2 (4.5%)	1 (5%)	1 (4.2%)	0.345	0.472	0.534
ASS	48 (76.2%)	14 (73.7%)	6 (60%)	8 (88.9%)	34 (77.3%)	14 (70%)	20 (83.3%)	0.759	0.584	0.692
Clopidogrel	6 (9.5%)	1 (5.3%)	1 (10%)	0	5 (11.4%)	1 (5%)	4 (16.7%)	0.449	0.605	0.191

Data are presented as absolute frequencies (percentages). The *P* values are presented for all procedures SAPT *versus* DAPT and SAPT *versus* DAPT for fEVAR and bEVAR patients separately, applying Student's *t*-test, Mann-Whitney-U, or chi^2 test where applicable.
ACE-Blocker = angiotensin converting enzyme- blocker; CCB = calcium chanel blocker; SAPT = single antiplatelet therapy; DAPT = dual antiplatelet therapy; fEVAR = fenestrated endovascular aortic repair; bEVAR = branched endovascular aortic repair.

Endovascular treatment

Branched and fenestrated stent graft devices were used from two different companies (Supplementary Fig. 1A). Overall TV treatment included a total of 120 branches and 90 fenestrations. In most cases, all 4 TVs of the reno-visceral segment were treated (Table 4). Aortic zone 5 was the most common proximal landing zone of all implanted devices in all groups, while the distal landing zone was mostly in zone 10. Throughout the study groups, mono-iliac devices were rarely deployed (Table 5).

Primary and secondary outcomes

Patient overall survival was 95% (±5.1) for SAPT and 88% (±8.8) for DAPT after 36 mo FU applying Kaplan–Meier estimator (n.s.) (Fig. 1D). Total FU was 76 mo, but the analysis in the following will only focus on the 36 mo FU data given the highly reduced data availability at later time points. The mean FU in the whole cohort was 15 mo. When analyzing the survival rates at after 36 mo for bEVAR and fEVAR patients separately, a survival rate of 100% (±0) for SAPT and 80% (±17.9) for DAPT (n.s.) was observed in patients treated with bEVAR and of 90% (±9.5) for SAPT and 95% (±5.2) for DAPT (n.s.) in patients treated with fEVAR (Fig. 1E and F). In total, two patients died due to aorta-related or procedure-related causes during FU ($n = 1$ stent migration and rupture; $n = 1$ postoperative bleeding).

Next, we analyzed the freedom from EL during the FU. Here, we report a freedom from any EL of 35% (±13.7) for SAPT *versus* 30% (±13.8) for DAPT for the entire study cohort at 36 mo FU (n.s.) (Fig. 2A). In the detailed evaluation, we observed a freedom from any EL rate of 33% (±18.4) for SAPT and 22% (±17.0) for DAPT in the bEVAR and of 36% (±20.1) for SAPT and 39% (±17.8) for DAPT in the fEVAR subgroup (Fig. 2B and C). All of these were diagnosed during postprocedural imaging. In total, we found a total of 41 EL in 29 patients, which corresponds to an overall EL rate of 46%. Of these, 14 were type III endoleaks (TIIIEL) in a total of 12 patients, which corresponds to an overall TIIIEL rate of 19% ($n = 13$ TIIIdEL; $n = 1$ TIIIbEL), all of which were diagnosed during postprocedural FU imaging. When applying the Kaplan–Meier estimator, we found a TIIIEL of 58 (±19.8) % for SAPT and 58 (±18.4) % for DAPT in the bEVAR and of 80 (±17.9) % for SAPT and 77 (±15.3) % for DAPT in the fEVAR-treated patients (Fig. 2D and E). We found a total of four type I endoleak (TIEL, 6%, $n = 2$ TIaEL and $n = 2$ TIbEL).

Aside EL formation, TV patency was another endpoint of utmost interest. We found no significant differences in SAPT *versus* DAPT for patency of the CT [100% (±0) *versus* 87% (±9.6)], SMA [86% (±13.2) *versus* 100% (±0)], LRA [92% (±8.0) *versus* 95% (±3.6)], or RRA [72% (±15.2) *versus* 81% (±9.9)] occlusion (Fig. 3A-D). This was also the case when analyzing all TV-specific patency rates for fEVAR and bEVAR separately (Supplementary Fig. 2A-E; Supplementary Fig. 3A-E). Treatment in an emergency or urgent setting did not critically affect TV patency ($n = 1$ CT occlusion; $n = 1$ SMA occlusion; $n = 1$ RRA occlusion). Further, we did not observe significant differences for complications other than EL and TV occlusion, including bleeding, impaired wound healing, or limb occlusion, when comparing SAPT *versus* DAPT in the bEVAR and fEVAR cohort (Table 4, Supplementary Fig. 1B).

Since we did not observe major differences regarding the major outcome parameters between SAPT *versus* DAPT following bEVAR and fEVAR, we evaluated whether aortic anatomical- or bridging stent graft-related parameters may have affected the postsurgical procedure-specific outcomes using univariate logistic regression. Here, neither TV-related anatomical nor bridging stent graft-related parameters were found to predict TV patency (Supplementary Table 2). In addition, we performed logistic regression analysis evaluating antiplatelet therapy regime with regard to overall EL

Table 3 – Aneurysm characteristics.

Characteristics	Total cohort	SAPT			DAPT			*P* value		
	($n = 63$)	Overall ($n = 19$)	fEVAR ($n = 10$)	bEVAR ($n = 9$)	Overall ($n = 44$)	fEVAR ($n = 20$)	bEVAR ($n = 24$)	SAPT *versus* DAPT	SAPT fEVAR *versus* DAPT fEVAR	SAPT bEVAR *versus* DAPT bEVAR
Symptomatic	9 (14.3%)	4 (21.1%)	3 (30%)	1 (11.1%)	4 (9.2%)	1 (5%)	3 (12.5%)	0.191	0.058	0.913
Ruptured	4 (6.3%)	0	0	0	1 (2.3%)	1 (5%)	0	0.508	0.472	/
PAU	6 (9.5%)	1 (5.3%)	1 (10%)	0	2 (4.5%)	1 (5%)	1 (4.2%)	0.902	0.605	0.534
TBAD	6 (9.5%)	3 (15.8%)	1 (10%)	2 (22.2%)	3 (6.8%)	1 (5%)	2 (8.3%)	0.266	0.605	0.276
Juxtarenal AAA	20 (31.7%)	1 (5.3%)	0	1 (11.1%)	6 (13.6%)	2 (10%)	4 (16.7%)	0.332	0.301	0.692
TAA Crawford classification										
Crawford 1	1 (1.6%)	0	0	0	0	0	0	/	/	/
Crawford 2	15 (23.8%)	1 (5.3%)	0	1 (11.1%)	2 (4.5%)	1 (5%)	1 (4.2%)	0.902	0.472	0.457
Crawford 3	5 (7.9%)	3 (15.8%)	3 (30%)	0	3 (6.8%)	1 (5%)	2 (8.3%)	0.266	0.058	0.372
Crawford 4	32 (50.8%)	1 (5.3%)	1 (10%)	0	1 (2.3%)	0	1 (4.2%)	0.534	0.150	0.534
Crawford 5	5 (7.9%)	4 (21.1%)	0	4 (44.4%)	5 (11.4%)	2 (10%)	3 (12.5%)	0.313	0.301	**0.046**
Aneurysm anatomy										
Maximum aortic diameter mm	60.9 ± 9.44	68.58 ± 7	51.6 ± 8.04	63.67 ± 7.2	62.45 ± 9.01	60.7 ± 10	63.92 ± 8.01	0.154	**0.027**	0.640
Maximum diameter proximal neck (mm)	28.71 ± 6.21	30.23 ± 7.89	25.29 ± 3.59	36 ± 7.72	28.21 ± 5.58	25.17 ± 5.34	30.81 ± 4.41	0.735	0.903	0.075
	($n = 52$)	($n = 13$)	($n = 7$)	($n = 6$)	($n = 39$)	($n = 18$)	($n = 21$)			
Maximum diameter distal neck (mm)	**24.0 (24.25-33.0)**	**22.0 (20.0-27.0)**	**22.0 (20.0-23.0)**	**26.0 (20.0-30.0)**	**25.0 (21.75-28.0)**	**24.0 (21.0-27.0)**	**26.0 (23.0-31.0)**	0.149	0.162	0.623
	($n = 56$)	($n = 14$)	($n = 7$)	($n = 7$)	($n = 42$)	($n = 19$)	($n = 23$)			
Maximum pathology length. (cm)	**15.47 (11.98-21.75)**	**14.52 (11.81-30.09)**	**12.47 (9.18-30.75)**	**19.43 (14.38-32.57)**	**16.21 (13.01-21.33)**	**13.26 (10.46-14.98)**	**20.97 (16.52-26.6)**	0.920	0.868	0.953
	($n = 53$)	($n = 14$)	($n = 8$)	($n = 6$)	($n = 39$)	($n = 18$)	($n = 21$)			

Data are presented as absolute frequencies (percentages) or mean ± standard deviation (SD) as indicated as roman or median and quartiles (Q1+3) for non-normally distributed continuous data as indicated as bold. The *P* values are presented for all procedures SAPT *versus* DAPT and SAPT *versus* DAPT in fEVAR and bEVAR patients separately, applying Student's *t*-test, Mann-Whitney-*U*, or chi^2 test where applicable.

PAU = Penetrating aortic ulcer; TBAD = Type B aortic dissection; AAA = Abdominal aortic aneurysm; TAA = Thoracic abdominal aortic aneurysm; SAPT = single antiplatelet therapy; DAPT = dual antiplatelet therapy; fEVAR = fenestrated endovascular aortic repair; bEVAR = branched endovascular aortic repair.

Table 4 – Postprocedural complications.

Complications	Total cohort	SAPT			DAPT			P value		
	(*n* = 63)	Overall (*n* = 19)	fEVAR (*n* = 10)	bEVAR (*n* = 9)	Overall (*n* = 44)	fEVAR (*n* = 20)	bEVAR (*n* = 24)	SAPT *versus* DAPT	SAPT fEVAR *versus* DAPT fEVAR	SAPT bEVAR *versus* DAPT bEVAR
Major bleeding	8 (12.7%)	4 (21.1%)	3 (30%)	1 (11.1%)	4 (9.2%)	1 (5%)	3 (12.5%)	0.191	0.058	0.913
Infection	1 (1.6%)	0	0	0	1 (2.3%)	1 (5%)	0	0.508	0.472	/
Cardiovascular	3 (4.8%)	1 (5.3%)	1 (10%)	0	2 (4.5%)	1 (5%)	1 (4.2%)	0.902	0.605	0.534
Neurologic	6 (9.5%)	3 (15.8%)	1 (10%)	2 (22.2%)	3 (6.8%)	1 (5%)	2 (8.3%)	0.266	0.605	0.276
Nephrological	7 (11.1%)	1 (5.3%)	0	1 (11.1%)	6 (13.6%)	2 (10%)	4 (16.7%)	0.332	0.301	0.692
Pulmonary	0	0	0	0	0	0	0	/	/	/
Delayed wound healing	3 (4.8%)	1 (5.3%)	0	1 (11.1%)	2 (4.5%)	1 (5%)	1 (4.2%)	0.902	0.472	0.457
Stent migration	6 (9.5%)	3 (15.8%)	3 (30%)	0	3 (6.8%)	1 (5%)	2 (8.3%)	0.266	0.058	0.372
Stent material failure	2 (3.2%)	1 (5.3%)	1 (10%)	0	1 (2.3%)	0	1 (4.2%)	0.534	0.150	0.534

Data are presented as absolute frequencies (percentages). The *P*-values are presented for all procedures SAPT *versus* DAPT and SAPT *versus* DAPT for fEVAR and bEVAR patients separately, applying Student's *t*-test, Mann-Whitney-*U*, or chi^2 test where applicable.
SAPT = single antiplatelet therapy; DAPT = dual antiplatelet therapy; fEVAR = fenestrated endovascular aortic repair; bEVAR = branched endovascular aortic repair.

formation and overall TV patency with and without adjusting for pathology and disease-related risk factors. Again, no significant association was found for both outcome parameters with and without risk adjustment (Supplementary Fig. 3).

Discussion

In the present study, we compared major outcome parameters after complex aortic endovascular repair by bEVAR and fEVAR in patients receiving either SAPT or DAPT following surgery.

Comprehensively, we found no significant differences in survival, EL incidence, and TV patency rates during FU between the two treatment groups. In addition, TV-related anatomical and bridging stent graft-related parameters did not affect TV patency in regression analysis. Our results therefore suggest the significance of the interaction of different and partly patient-specific factors for patient outcome rather than the form of antiplatelet therapy chosen after endovascular repair.

While recent guidelines promote complex aortic endovascular repair as well-established alternative to conventional open surgical repair for pathologies affecting the reno-visceral segment in patients with suitable anatomy and especially high-risk profile, the guidelines make no recommendations regarding the postsurgical antiplatelet medication regimen.[20] Therefore, the decision on whether to use SAPT or DAPT and the duration of such medication following complex endovascular aortic procedures is based on the surgeon's experience and preference rather than on scientific evidence. Given that these endovascular techniques have been in use for more than two decades, this status quo appears unsatisfying.

A recent study tried to address this issue by asking 77 international experts regarding pre-, intra-, and postoperative management of antithrombotic therapy in elective bEVAR and fEVAR patients to reach a Delphi consensus for treatment recommendations. While there was strong consent on the use of postsurgery SAPT in bEVAR and fEVAR patients in general, the initiation of a DAPT for patients that did not receive DAPT for other comorbidities was more controversial in some aspects. For instance, views on the duration of DAPT medication, which ranged from one to 6 mo, as well as a possible lifetime DAPT in case of tortuous anatomy or multiple bridging stent graft implantations, were a controversial point of discussion.[21] Nevertheless, the authors noted the the lack of data regarding the use of DAPT in these patients and underlined the need for clinical data to support evidence-based decision-making.

Indeed, studies evaluating the use of antiplatelet medication following complex aortic endovascular repair are sparse. Interestingly, the antiplatelet medication does not appear to alter the rate of TIIEL, since a recent metanalysis that included 45 studies with a total of over 35.000 patients found no association between TIIEL onset and antiplatelet medication.[22] Another study found an outcome-based benefit of DAPT, such as a lower limb occlusion rate, with no increase in the overall complication rate, which points to a potential benefit of DAPT after endovascular aortic procedures.[23] This is further supported by a study by Fan *et al.*, which found no differences in bleeding complications, survival, or reintervention rates among different anticoagulant or antiplatelet regimens, but higher 1-y TV patency with postprocedural DAPT in a big cohort of over 1500 patients undergoing bEVAR or fEVAR.[24] While in our study we could not identify such benefit, DAPT was also not associated with a higher incidence of complication or survival disadvantage.

In contrast, a recent study reported 1-y outcomes in 1291 patients undergoing complex endovascular aortic aneurysm

Table 5 – Stent graft features.

Stent graft-related features	Total cohort	SAPT		DAPT	
	($n = 63$)	fEVAR ($n = 10$)	bEVAR ($n = 9$)	fEVAR ($n = 20$)	bEVAR ($n = 24$)
Total number of branches	120	-	32	-	88
1	2 (5.9%)	-	0	-	1 (4.2%)
2	0	-	0	-	0
3	10 (29.4%)	-	4 (44.4%)	-	6 (25%)
4	22 (64.7%)	-	5 (55.6%)	-	17 (70.8%)
Total number of fenestrations	90	35	-	55	-
1	2 (6.7%)	1 (10%)	-	1 (5%)	-
2	8 (26.7%)	4 (40%)	-	4 (20%)	-
3	8 (26.7%)	2 (20%)	-	6 (30%)	-
4	12 (40%)	3 (30%)	-	9 (45%)	-
Proximal zone of attachment	($n = 46$)	($n = 8$)	($n = 6$)	($n = 13$)	($n = 19$)
Zone 2	1 (1.6%)	0	0	0	1 (5.3%)
Zone 3	5 (7.9%)	1 (12.5%)	1 (16.7%)	0	3 (15.8%)
Zone 4	8 (12.7%)	0	1 (16.7%)	3 (23.1%)	4 (21.1%)
Zone 5	26 (41.3%)	4 (50%)	4 (66.7%)	7 (53.8%)	11 (57.9%)
Zone 6	3 (4.8%)	0	0	3 (23.1%)	0
Zone 7	3 (4.8%)	3 (37.5%)	0	0	0
Distal zone of attachment	($n = 46$)	($n = 8$)	($n = 6$)	($n = 13$)	($n = 19$)
Zone 5	1 (1.6%)	1 (12.5%)	0	0	0
Zone 7	2 (3.2%)	0	0	1 (7.7%)	1 (5.3%)
Zone 9	14 (22.2%)	2 (25%)	2 (33.3%)	2 (15.4%)	8 (42.1%)
Zone 10	28 (44.4%)	5 (62.5%)	3 (50%)	10 (76.9%)	10 (52.6%)
Zone 11	1 (1.6%)	0	1 (16.7%)	0	0
Biiliacal	27 (42.97%)	5 (62.5%)	4 (66.7%)	9 (69.2%)	9 (47.4%)
	($n = 46$)	($n = 8$)	($n = 6$)	($n = 13$)	($n = 19$)
Monoiliacal	2 (4.3%)	0	0	1 (5%)	1 (5.3%)
	($n = 46$)	($n = 8$)	($n = 6$)	($n = 13$)	($n = 19$)

Data are presented as absolute frequencies (percentages) for individual groups. The *P*-values are presented for all procedures SAPT *versus* DAPT and SAPT *versus* DAPT in fEVAR and bEVAR patients separately, applying Student's *t*-test, Mann-Whitney-*U*, or chi^2 test where applicable.
SAPT = single antiplatelet therapy; DAPT = dual antiplatelet therapy; fEVAR = fenestrated endovascular aortic repair; bEVAR = branched endovascular aortic repair.

procedures with respect to either SAPT or DAPT and found no differences between both medication regimens in regard to aneurysm diameter progression, the need of reintervention, and vessel-specific reintervention rates. Of note, the number of patients discharged on DAPT increased steadily during the study period.[17,25] Unfortunately, the data are not yet available as a full-length manuscript and do not report on the separate outcomes of bEVAR and fEVAR patients. Our results comprehensively support those findings and add an even more precise perspective. Beside this, there are multiple studies that report on the outcomes following bEVAR or fEVAR but unfortunately do not evaluate the postsurgery antiplatelet therapy regimen as a potential contributor to major outcome parameters.[7,26-28]

Unlike most studies on this topic, our study reports outcomes for antiplatelet therapy regimen following bEVAR and fEVAR separately for each procedure. Although we could not observe differences with either medication regime regarding TV patency and EL rates, we also did not find increased incidence of major bleedings or impaired wound healing for DAPT. This is in line with data from He *et al.*, who found no increase in hemorrhage, EL rates, recurrent dissection, death, and myocardial infarction in type B aortic dissection and coronary heart disease patients on DAPT who underwent EVAR, suggesting a sufficient overall safety of DAPT in this patient cohort.[29]

In addition, we could not identify anatomical or bridging stent graft-related parameters that may have affected TV patency aside from the antiplatelet therapy, while other studies identified TV tortuosity to independently affect EL but not TV patency rates.[30] Albeit the significance of TV tortuosity seems somewhat conclusive for the TV-specific patient

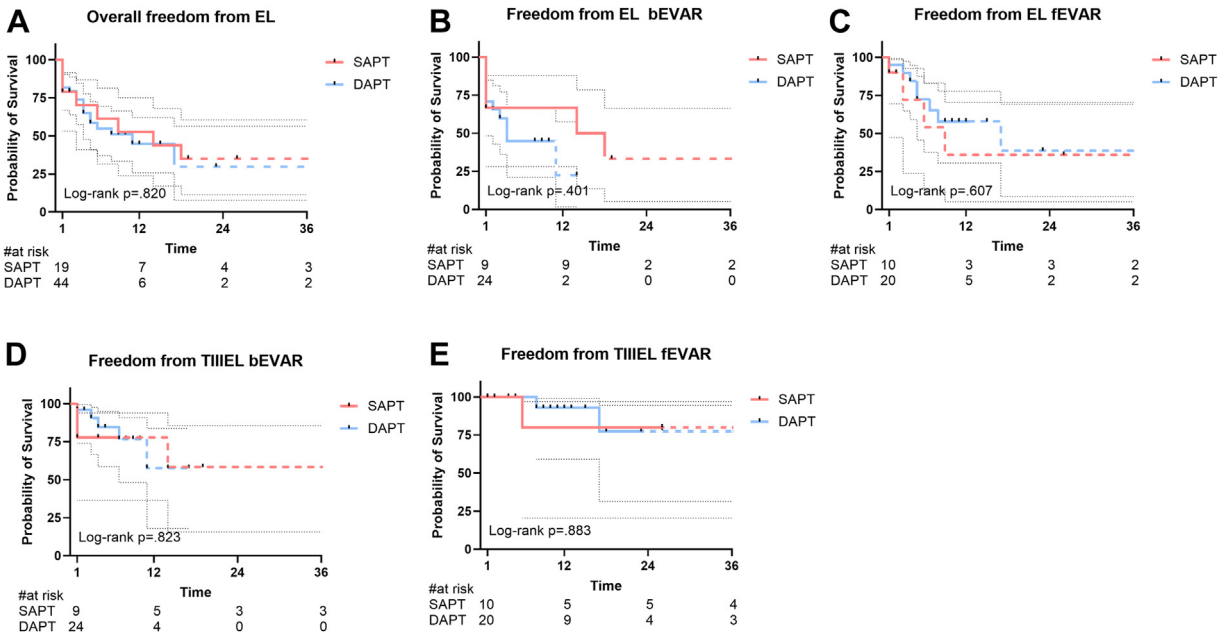

Fig. 2 – Kaplan–Meier estimates for freedom from EL. Overall freedom from all EL in SAPT *versus* DAPT in the whole study cohort (A) and in fEVAR (B) and bEVAR (C) patients separately. TIIIEL was further assessed separately for fEVAR (D) and bEVAR (E) patients on postprocedural SAPT *versus* DAPT. Kaplan–Meier estimates displayed with 95% CI. *P* value of log-rank test displayed in the graph. EL = endoleak; bEVAR = branched endovascular aortic repair; fEVAR = fenestrated endovascular aortic repair; SAPT = single antiplatelet therapy; DAPT = dual antiplatelet therapy; TIIEL = type III endoleak; # = number.

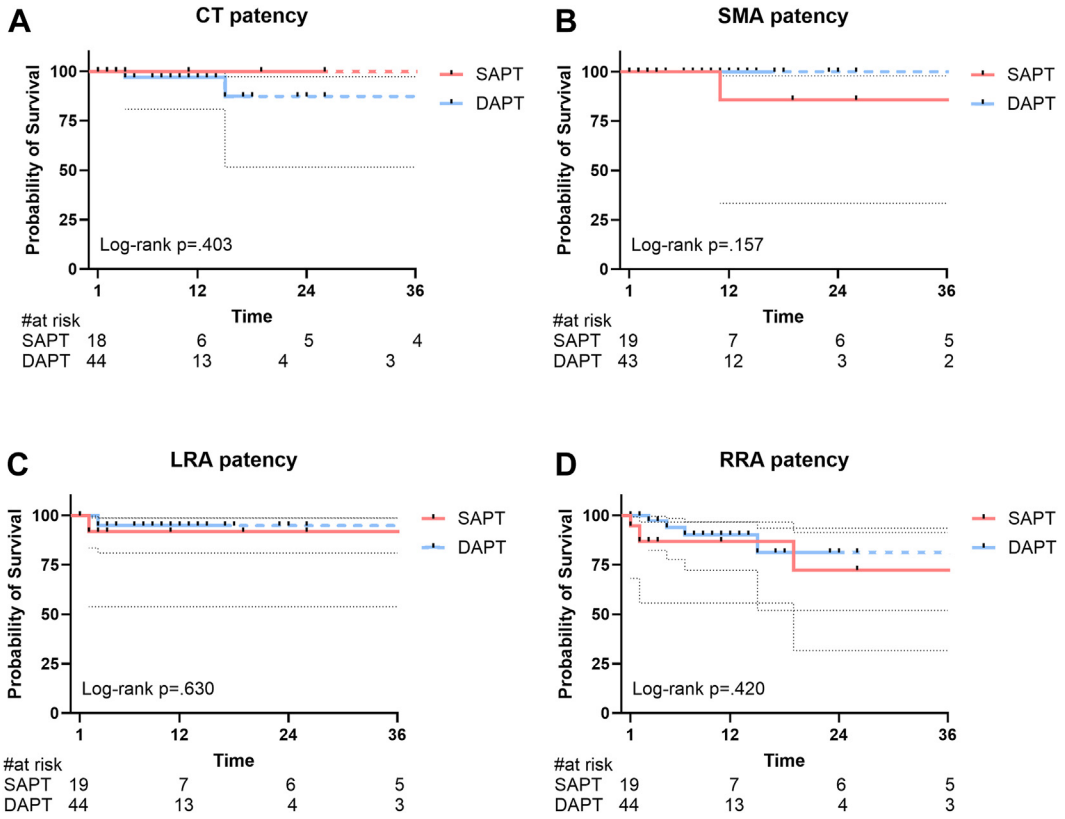

Fig. 3 – Kaplan–Meier estimates for TV patency. Patency of individual TV bEVAR and fEVAR patients combined comparing SAPT *versus* DAPT (A-D). Kaplan–Meier estimates displayed with 95% CI. *P* value of log-rank test displayed in the graph. TV = target vessel; CT = celiac trunk; SMA = superior mesenteric artery; LRA = left renal artery; RRA = right renal artery; SAPT = single antiplatelet therapy; DAPT = dual antiplatelet therapy; # = number.

outcome, this potential influencing variable was not in the scope of the present study. Therefore, the anatomic parameters can also not explain the admittedly high rate of RRA TV occlusion, which was observed in this series. Further, final confirmation of patency during the procedure was performed by angiogram, while more recent studies also suggest adjunctive, supportive techniques like intravascular ultrasound to improve bridging stent graft placement.[31]

We consider postoperative antiplatelet therapy to be decisive for the outcome for mechanistically comprehensible reasons. There is accumulating evidence that the implantation of stent grafts into the aortic lumen has major effects on platelet counts and activity.[32] Several platelet activity markers are increased following EVAR, a condition that persists for several weeks.[33-35] For this reason, there is a general recommendation for antiplatelet therapy to reduce the likelihood of clot formation and to prevent TV or limb occlusion regardless of the extent of aortic coverage or adjunctive vessel treatment.[20] However, based on the available data to date, it cannot be specified whether one of the available antiplatelet agents is superior to the others or whether DAPT can provide additional beneficial effects.[36]

This applies to both following EVAR but especially after bEAVR or fEVAR procedures. Noteworthy, several studies have been published that clearly demonstrate the heterogeneity in patient-specific responses to different antiplatelet agents and regimens.[37] Despite the fact that several laboratory testing methods are commonly available, potential beneficial effects of their implementation into the daily routine to track the patient-specific response of the applied antiplatelet therapy have yet to be demonstrated.[38] That said, we would like to motivate the initiation of precisely these studies and believe that a high benefit could be generated for the patients concerned.

Our study has several major limitations. Due to the retrospective study design, we lost numerous cases during FU, which limits the validity of the data at later FU time points. In addition, only two centers participated in the study, further limiting the total number of patients.

It needs to be further noted that in our cohort, SAPT was used in almost half the cases. We are aware of the fact, that this does not resemble the current state of the art anymore, but it is due to the fact that at one center, the data for this study was collected throughout a time span of several years. During that time, not only did the learning curve in the use of the endovascular devices implanted by different surgeons evolve, but also did the institutional standard for postsurgery antiplatelet therapy with an increased use of DAPT over time. Given the retrospective study design, the indication for SAPT only is not traceable for most cases anymore. Of note, we did not differentiate between preprocedural SAPT in terms of whether Clopidogrel or ASS was used, as a differential consideration would have further reduced the sample size of our study groups. However, 4 of 24 patients in the bEVAR group who were treated postoperatively with DAPT were on clopidogrel preop, which may have affected outcomes compared to the other groups and potentially would have made a difference in a larger study group. We also excluded patients with postsurgery oral anticoagulation regimes to focus only on the effects of antiplatelet therapy, yet oral anticoagulation is also frequently used and should therefore be included in future analysis. It needs to be noted that we observed a high incidence of overall EL with a particularly high rate of TIIIEL compared to other studies, which report ~4% TIIIEL for complex f/bEVAR.[39,40] his may partly be attributed to a center-specific focus on only one type of bridging stent graft during the study period, which does not represent the wide range of overall available products and represents a limitation for the transferability of the reported data.

Further, our study cohort provides no information regarding efficiency testing of SAPT/DAPT therapy, because in both institutions, such testing has only been introduced to clinical routine in the recent past. This may have biased results reported herein, and therefore, the generalizability of our observations is not possible without restrictions, and findings should be interpreted conservatively.

In summary, we did not observe significant differences between postsurgical SAPT *versus* DAPT in several outcome parameters after complex aortic endovascular procedures, as well as in a separate consideration for bEVAR and fEVAR procedures. Also, the herein examined anatomical conditions of the aorta or bridging stent graft-specific parameters did not predict TV patency. Conclusively, the interplay of several factors, which may differ significantly between individual patients, may be far more important for the outcome than previously assumed and more important than solely focusing on single aspects like the antiplatelet therapy regime. In any case, further studies are needed to increase the data availability for evidence-based decision-making going forward.

Supplementary Materials

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jss.2024.11.018.

Disclosure

The authors declare no conflict of interest.

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CRediT authorship contribution statement

Joscha Mulorz: Writing – original draft, Visualization, Supervision, Methodology, Investigation, Data curation, Conceptualization. **Laura M. Costanza:** Writing – review & editing, Investigation. **Malwina Vockel:** Investigation, Data curation. **Agnesa Mazrekaj:** Writing – review & editing, Visualization, Methodology, Investigation. **Amir Arnautovic:** Writing – review & editing, Visualization, Methodology. **Waseem Garabet:** Writing – review & editing, Methodology, Conceptualization.

Alexander Oberhuber: Writing – review & editing, Supervision, Resources, Methodology, Data curation, Conceptualization. **Hubert Schelzig:** Writing – review & editing, Supervision, Resources, Conceptualization. **Markus U. Wagenhäuser:** Writing – original draft, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

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