

Role of Antiplatelet Therapy in Patients Managed for Complex Aortic Aneurysms using Fenestrated or Branched Endovascular Repair

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WHAT THIS PAPER ADDS

For the first time, this study of 1 430 patients has evaluated the role of double antiplatelet therapy (DAPT) vs. single antiplatelet therapy (SAPT) after fenestrated and branched endovascular aortic repair (F/B-EVAR). DAPT provided benefit in terms of cardiovascular ischaemic morbidity (SAPT 11.9% vs. DAPT 8.2%; $p = .040$), mainly driven by lower rates of acute mesenteric and limb ischaemia, without additional cost of post-operative major haemorrhagic events (SAPT 7.5% vs. DAPT 6.3%; $p = .40$). DAPT was related to higher target vessel patency at thirty six months (SAPT 93.4%, standard error [SE] 0.7% vs. DAPT 97.0%, SE 0.6%; log rank $p = .007$), especially in patients managed with B-EVAR.

Objective: Despite the increasing number of fenestrated and branched endovascular aortic repair (F/B-EVAR) procedures, evidence on post-operative antiplatelet therapy is very limited. This study aimed to investigate the role of single antiplatelet therapy (SAPT) vs. double antiplatelet therapy (DAPT) after F/B-EVAR in 30 day and follow up outcomes.

Methods: A multicentre retrospective analysis was conducted, including F/B-EVAR patients managed from 1 January 2018 to 31 December 2022. Comparative outcomes were assessed according to post-operative antiplatelet therapy. The cohort was divided into the SAPT group (acetylsalicylic acid [ASA] or clopidogrel) and DAPT group (ASA and clopidogrel). The duration of SAPT or DAPT was one to six months. Primary outcomes were 30 day death, and cardiovascular ischaemic and major haemorrhagic events. Secondary outcomes were survival and target vessel (TV) patency during follow up.

Results: A total of 1 430 patients were included: 955 under SAPT and 475 under DAPT. The 30 day mortality rate was similar (SAPT 2.1% vs. DAPT 1.5%; $p = .42$). Cardiovascular ischaemic events were lower in the DAPT group (SAPT 11.9% vs. DAPT 8.2%; $p = .040$), with DAPT being an independent protector for acute mesenteric ($p = .009$) and lower limb ischaemia ($p = .020$). No difference was found in 30 day major haemorrhagic events (SAPT 7.5% vs. DAPT 6.3%; $p = .40$). The mean follow up was 21.8 ± 2.9 months. Cox regression showed no survival confounders, with similar rates between groups (log rank $p = .71$). DAPT patients enjoyed higher TV patency (SAPT 93.4%, standard error [SE] 0.7% vs. DAPT 97.0%, SE 0.6%; log rank $p = .007$) at

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thirty six months. Cox regression revealed B-EVAR as a predictor of worse TV patency (hazard ratio 2.03, 95% confidence interval 1.36 – 3.03; $p < .001$). DAPT was related to higher patency within B-EVAR patients (SAPT 87.2%, SE 2.1% vs. DAPT 94.9%, SE 1.9%; $p < .001$).

Conclusion: DAPT after F/B-EVAR was associated with lower risk of cardiovascular ischaemic events and higher TV patency, especially in B-EVAR cases. No difference in major haemorrhagic events was observed at 30 days.

Keywords: Antiplatelet therapy, Aortic aneurysm, Branched, Endovascular repair, Fenestrated, Outcomes

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INTRODUCTION

Since the introduction of endovascular aortic aneurysm repair (EVAR) to clinical practice, the volume of cases managed with open surgical repair has decreased by 75%.¹ EVAR and complex endovascular aortic repair, such as fenestrated and branched endovascular aortic repair (F/B-EVAR), have gained popularity due to the early survival benefit compared with open procedures.^{2–4} However, cardiovascular morbidity remains an issue, with rates up to 10%.^{4–7} Additionally, freedom from target vessel (TV) instability and need for TV related re-intervention have been reported at 90% at sixty months.^{8,9} Anatomical and technical factors have been studied and provided potential explanations for TV related adverse events.^{10,11}

Evidence on antithrombotic therapy and its role in adverse events after F/B-EVAR is limited.¹² A recent Delphi expert consensus report suggested double antiplatelet therapy (DAPT) for one to six months after F/B-EVAR, which could be expanded even to a lifelong scheme for cases at high risk of TV occlusion.¹² However, the authors acknowledged that the published data are scarce and studies are needed to define the role of DAPT in F/B-EVAR.¹² A recent study showed that female patients managed with B-EVAR may benefit from post-operative DAPT in terms of death and spinal cord ischaemia (SCI).¹³

This study aimed to investigate the role of antithrombotic therapy in patients managed using F/B-EVAR in terms of 30 day death, cardiovascular ischaemic and major haemorrhagic events, and TV patency during midterm follow up.

METHODS

Study design

A multicentre retrospective analysis was conducted among 15 European aortic centres ([Supplementary Table S1](#)) following the STrengthening the Reporting of OBServational studies in Epidemiology (STROBE) statement.¹⁴ All patients were managed for degenerative thoraco-abdominal aortic aneurysm (TAAA), pararenal or juxtarenal aneurysms, or chronic aortic dissections using fenestrated (custom made) or branched (custom made or off the shelf) devices from 1 January 2018 to 31 December 2022. The cohort was divided according to post-operative antiplatelet therapy into the single antiplatelet therapy (SAPT) group receiving acetylsalicylic acid (ASA) or clopidogrel, and the DAPT group receiving ASA and clopidogrel. The clopidogrel dosage was 75 mg daily, while the dosage for ASA ranged from 75 – 100 mg according to each centre's

clinical practice and commercially available pharmaceutical products. The decision for the type of antiplatelet therapy (SAPT or DAPT) after F/B-EVAR relied upon the previous experience of the surgeon and the specific local protocols of each centre. Except the Delphi expert consensus,¹² which was published in 2022, no further information on the management of antiplatelet therapy after F/B-EVAR was available.

All patient data were de-identified and inserted into a common database. This study complied with the Declaration of Helsinki. Approval by the ethics committee was acquired from each centre according to local authorities. According to the current state law (§12 HmbKHG), no further approval was required from the local ethics committee of the responsible centre.

Inclusion and exclusion criteria

To increase the homogeneity of the cohort, only procedures performed with custom made or off the shelf devices relying on the Cook platforms (William Cook Europe, Bjaeverskov, Denmark) were eligible. The presence of fenestrations and or inner or outer branches was not considered an exclusion criterion. Patients managed with standard EVAR or any fenestrated or branched device other than the Zenith platform, and patients managed with surgeon modified grafts or the parallel graft technique were also excluded. Elective and symptomatic patients (non-ruptured aneurysm) were included. Cases managed for ruptured aneurysms or acute aortic dissections were excluded.

Patients' antithrombotic therapy on admission and discharge from the hospital, including the type (ASA, clopidogrel, or DAPT) were collected. All patients were taking antiplatelet therapy before F/B-EVAR with at least one antiplatelet agent (ASA and or clopidogrel). Nineteen patients were managed with DAPT post-operatively for reasons other than F/B-EVAR. Medication prescription for at least 30 days and up to six months was also collected when available. DAPT initiation was within 24 – 48 hours after repair, according to the treating physician's preference.

The following patients were excluded: those under treatment with any other antiplatelet (e.g., triflusal, ticagrelor, prasugrel, or cilostazol), in addition to patients taking a therapeutic dose of any anticoagulation (e.g., phenprocoumon, warfarin) or direct oral anticoagulants (e.g., rivaroxaban, apixaban, dabigatran); those taking low dose rivaroxaban in combination with SAPT or DAPT; those with a history of cancer (remote or active); and those with confirmed haematological or liver diseases.^{15–18}

Data collection

Pre-, intra-, and post-operative information was collected. The following post-operative 30 day outcomes were collected: death; cardiovascular ischaemic events (myocardial infarction [MI], minor or major ischaemic stroke, SCI [including Grade 1, 2, and 3 according to the Society for Vascular Surgery {SVS} reporting standards], acute mesenteric ischaemia, acute limb ischaemia); and any major haemorrhagic event according to the International Society on Thrombosis and Haemostasis (ISTH) modified criteria (fatal bleeding, symptomatic bleeding into a critical organ [intracranial, intra-articular, intramuscular with compartment syndrome, intra-ocular, respiratory, pericardial, liver, pancreas, retroperitoneal, adrenal gland, or kidney], and bleeding into a surgical site requiring re-operation).^{18,19} Access site haematomas, treated conservatively or by surgical management, were reported.

Patient surveillance protocols differed between centres. Follow up data included survival status (dead or alive), freedom from endoleak, and TV patency; they were assessed only among patients with confirmed medication prescription for at least one month (duration one to six months).

Definitions

The SVS reporting standards were applied for available definitions, including technical success.^{18,20} SCI was defined as any new onset post-operative neurological lower limb deficit, not attributable to any other pathology, up to 30 days after the procedure and was classified as Grade 1, 2, and 3 according to the SVS reporting standards.¹⁸ Cardiovascular ischaemic events included any post-operative MI, ischaemic stroke (minor or major), SCI of any grade (1, 2, and 3), acute mesenteric ischaemia, and acute limb ischaemia. MI was defined as the result of atherothrombotic coronary artery disease related to the detection of a rise or fall in troponin concentrations and at least one of the following criteria: (1) symptoms of acute myocardial ischaemia; (2) new ischaemic electrocardiographic changes or the development of pathological Q waves; (3) imaging evidence of a new loss of viable myocardium or new regional wall motion abnormality; and (4) identification of atherothrombosis by angiography or autopsy.²¹ Ischaemic stroke was defined as any neurological deficit attributed to cerebral infarction as the result of an acute focal injury of a vascular cause.¹⁸ A modified Rankin's score ≥ 3 was used to identify major stroke.²² Both intracerebral haemorrhage and subarachnoid haemorrhage were included in the haemorrhagic outcomes (intracranial haemorrhage).²² TV patency was considered as uninterrupted patency without occlusion or a procedure performed to maintain patency of the bridging stent or TV.¹⁸

Outcomes

Primary outcomes were comparative 30 day mortality rate, cardiovascular ischaemic events, and major haemorrhagic events according to the ISTH between the SAPT and DAPT

groups. Secondary outcomes were survival, endoleak, and TV patency during follow up.

Statistical analysis

Normally distributed continuous data were reported with mean \pm standard deviation, and non-normally distributed data as median with interquartile range and range values. Categorical data were expressed as absolute numbers and percentages. A comparative analysis between patients receiving SAPT or DAPT was performed using the Fisher's exact and Pearson's χ^2 test. The Mann–Whitney *U* test was used for non-normally distributed continuous variables. Uni- and multivariable analyses were performed to identify independent baseline characteristics related to the DAPT group and to investigate DAPT association with adverse events. Due to a lack of data in the literature on this specific topic, only statistical factors shown to provide significance at the univariable stage were included in the multivariable analysis. Kaplan–Meier estimates were performed to assess follow up survival, freedom from endoleak, and TV patency. To determine risk adjusted follow up outcomes, Cox proportional hazards models adjusting for these variables (chronic obstructive pulmonary disease [COPD], chronic heart failure [CHF], dyslipidaemia, and sex) were created for survival, endoleak, and TV patency. Despite not achieving significance within the multivariable analysis, factors that could potentially affect TV patency, such as device configuration (F-EVAR, B-EVAR), aneurysm type (TAAA, juxtarenal, pararenal), and the presence of dissection, were evaluated through Cox regression for this specific outcome. The log rank test was used to compare distributions. No correction for multiple hypothesis testing was applied. Missing data were random both for categorical and continuous variables ($< 5\%$) and they were not imputed. A *p* value was considered statistically significant when $< .050$. Statistical analysis was performed using IBM SPSS Statistics for iOS Version 29.0 software (IBM Corp., Armonk, NY, USA).

RESULTS

Patient cohort

A total of 1 430 patients were included: 955 under SAPT and 475 under DAPT. The American Society of Anesthesiologists score (ASA score) III – IV rates were similar between groups (SAPT 91.6% vs. DAPT 91.1%; *p* = .76). The comparative pre-operative characteristics are presented in [Table 1](#). Multivariable analysis of baseline characteristics showed that patients taking DAPT had higher COPD (odds ratio [OR] 1.8, 95% confidence interval [CI] 1.4 – 2.3; *p* < .001), CHF (OR 0.5, 95% CI 0.36 – 0.80; *p* = .002), and dyslipidaemia (OR 2.0, 95% CI 1.6 – 2.5; *p* < .001) rates and were more commonly male (OR 1.5, 95% CI 1.1 – 2.0; *p* = .010) ([Table 1](#))

Primary 30 day outcomes

In terms of 30 day death, no difference was recorded between groups (SAPT 2.1% vs. DAPT 1.5%; *p* = .42). However, cardiovascular ischaemic events were less frequent in the

Table 1. Comparative baseline characteristics and multivariable regression analysis according to the post-operative antiplatelet treatment of single antiplatelet therapy (SAPT; $n = 955$) vs. double antiplatelet therapy (DAPT; $n = 475$) of patients managed with fenestrated and branched endovascular aortic repair.

Variable	SAPT ($n = 955$)	DAPT ($n = 475$)	p value	Univariable (p value)	Multivariable OR (95% CI)
Age – y	72.1 ± 8.3	71.6 ± 7.8	.64		
Male sex	763 (80.1)	402 (84.6)	.040	.010	1.5 (1.1–2.0); $p = .010$
Tobacco use	655 (68.6)	359 (75.9)	.006	.15	–
Active tobacco use	275 (28.8)	171 (36.2)	.006	.52	–
Hypertension	838 (87.7)	408 (85.9)	.32	–	–
Diabetes mellitus	156 (16.3)	76 (16.0)	.87	–	–
Dyslipidaemia	491 (51.4)	323 (68.0)	<.001	<.001	2.0 (1.6–2.5); $p < .001$
Coronary artery disease	360 (37.7)	203 (42.7)	.070	–	–
Myocardial infarction	112 (15.2)	92 (20.2)	.030	.19	–
CABG	71 (9.6)	44 (9.6)	.99	–	–
Percutaneous coronary intervention	131 (17.8)	97 (21.3)	.14	–	–
Chronic heart failure	108 (11.3)	36 (7.6)	.030	.002	0.5 (0.36–0.80); $p = .002$
COPD	277 (23.9)	180 (38.0)	<.001	<.001	1.8 (1.4–2.3); $p < .001$
Chronic kidney disease	248 (26.0)	118 (24.9)	.65	–	–
Dialysis	11 (1.2)	4 (0.8)	.59	–	–
Stroke	108 (11.3)	56 (11.8)	.79	–	–
Major	16 (2.2)	15 (3.3)	.24	–	–
Peripheral arterial disease	174 (18.2)	88 (18.5)	.89	–	–
Prior aortic repair	311 (32.7)	118 (24.8)	.002	.060	–
Symptomatic aneurysm	76 (8.0)	32 (6.7)	.41	–	–
Thoraco-abdominal aneurysm	331 (34.7)	186 (39.2)	.090	–	–
Chronic dissection	102 (11.0)	39 (8.2)	.14	–	–
Device design				.26	–
Branched device	359 (37.6)	150 (31.6)	.030	–	–
Fenestrated device	545 (57.1)	299 (62.9)	.030	–	–
Fenestrated and branch configuration	51 (5.3)	26 (5.5)	.92	–	–

Data are shown as n (%) or mean ± standard deviation. SAPT = single antiplatelet therapy; DAPT = double antiplatelet therapy; OR = odds ratio; CI = confidence interval; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease.

DAPT group (SAPT 11.9% vs. DAPT 8.2%; $p = .040$), including a statistically significant difference in acute mesenteric ischaemia (SAPT 1.9% vs. DAPT 0.2%; $p = .009$) and acute limb ischaemia (SAPT 2.7% vs. DAPT 0.6%; $p = .008$). No acute mesenteric ischaemia events were related to superior mesenteric artery (SMA) bridging stent occlusion on the pre-discharge computed tomography angiography. Seven events were related to distal SMA dissection, and the remaining were related to distal SMA branch embolisation. For acute limb ischaemia events, the type of access was not related to adverse events, as 2.1% acute limb ischaemic events were recorded in patients exclusively managed with femoral artery cut downs, 2.2% in patients managed with unilateral open access and contralateral percutaneous access, and 2.0% in patients exclusively managed with percutaneous access ($p = .98$). Among 29 acute limb ischaemia events, nine were related to local external iliac and or common femoral artery dissection, eight to common femoral artery thrombosis, nine to iliac occlusion, and three to distal embolisation.

After multivariable analysis, including the pre-operative statistically significantly different factors (COPD, CHF, dyslipidaemia, and sex), DAPT was identified as an independent protector for acute mesenteric and lower limb ischaemia (OR 0.12, 95% CI 0.02 – 0.93; $p = .009$; and OR 0.23, 95% CI 0.07 – 0.79; $p = .020$, respectively). For acute mesenteric ischaemia, no other cofactor affecting outcomes was

detected. For acute limb ischaemia, sex was also identified as a cofactor related to a higher rate of adverse events (OR 0.34, 95% CI 0.16 – 0.72; $p = .005$) (Supplementary Table S2). No difference was found in terms of MI, stroke, and SCI and the use of DAPT. The comparative 30 day outcomes are presented in Table 2.

Regarding the haemorrhagic events, no difference was found in terms of ISTH major haemorrhagic events (SAPT 7.5% vs. DAPT 6.3%; $p = .40$). The only statistically significant difference was found on access site haemorrhagic events needing conservative management, which were more common among the SAPT group (SAPT 6.0% vs. DAPT 2.2%; $p = .003$). No other factor was independently related to access site haemorrhagic events needing conservative management (Supplementary Table S2). The distribution of the haemorrhagic events is presented in Table 3.

Endoleak and target vessel patency at 30 days

For any type of endoleak within 30 days, no statistically significant difference was detected between groups (SAPT 37.6% vs. DAPT 39.1%; $p = .61$), either when separately evaluating type I (SAPT 4.0% vs. DAPT 2.9%; $p = .12$) or type III (SAPT 5.6% vs. DAPT 6.5%; $p = .76$) endoleaks. For type II endoleaks, the rate was 25.3% within the SAPT group and 29.2% within the DAPT group ($p = .17$). TV patency was similar between groups (SAPT 97.2% vs. DAPT 97.2%; $p = .94$).

Table 2. Distribution of post-operative cardiovascular ischaemic adverse events at 30 days according to post-operative antiplatelet treatment of single antiplatelet therapy (SAPT; $n = 955$) vs. double antiplatelet therapy (DAPT; $n = 475$) in patients managed with fenestrated and branched endovascular aortic repair, and multivariable analysis confirming the independent protective role of DAPT in acute mesenteric and limb ischaemia.

Variable	SAPT ($n = 955$)	DAPT ($n = 475$)	p value	Multivariable analysis OR (95% CI)
Cardiovascular ischaemic events	114 (11.9)	39 (8.2)	.040	0.7 (0.46–1.02); $p = .060$
Myocardial infarction	15 (1.6)	10 (2.1)	.47	–
Ischaemic stroke	18 (1.9)	4 (0.8)	.13	–
Major stroke	4 (0.4)	1 (0.2)	.53	–
Acute mesenteric ischaemia	18 (1.9)	1 (0.2)	.009	0.12 (0.02–0.93); $p = .009$
Need for bowel resection	10 (1.0)	1 (0.2)	.090	–
Acute limb ischaemia	26 (2.7)	3 (0.6)	.008	0.23 (0.07–0.79); $p = .020$
Spinal cord ischaemia	55 (5.8)	26 (5.5)	.83	–
Grade 3	17 (1.8)	6 (1.3)	.46	–

Data are shown as n (%). SAPT = single antiplatelet therapy; DAPT = double antiplatelet therapy; OR = odds ratio; CI = confidence interval.

Follow up outcomes

In 931 patients, the medical prescription of SAPT or DAPT for at least 30 days (one to six months) was retrieved from medical records and registered in the database. Among these patients, 540 were in the SAPT group and 391 in the DAPT group. The mean follow up was 21.8 ± 2.9 months, with no statistically significant between group difference ($p = .79$). The estimated survival was 84.3% (standard error [SE] 2.3%) for the SAPT group and 85.2% (SE 2.6%) for the DAPT group (log rank $p = .71$; Fig. 1) at thirty six months. After performing Cox regression analysis, defining COPD (hazard ratio [HR] 0.9, 95% CI 0.6 – 1.6; $p = .79$), CHF (HR 1.3, 95% CI 0.72 – 2.7; $p = .33$), dyslipidaemia (HR 1.2, 95% CI 0.78 – 1.8; $p = .45$), and sex (HR 1.0, 95% CI 0.66 – 1.6; $p = .91$) as cofactors, none was found to affect long term survival.

The freedom from endoleak was 79.4% (SE 2.4%) for the SAPT group and 73.7% (SE 3.1%) for the DAPT group at thirty six months (log rank $p = .040$) (Supplementary Fig. S1), with a freedom from type II endoleak at 79.5% (SE 2.4%) for the SAPT vs. 72.6% (SE 3.2%) for the DAPT group (log rank $p = .040$). After performing Cox regression analysis, defining COPD (HR 1.1, 95% CI 0.83 – 1.5; $p = .48$), CHF (HR 0.47, 95% CI 0.23 – 0.95; $p = .40$), dyslipidaemia (HR 1.0, 95% CI 0.8 – 1.3; $p = .87$), and sex (HR 1.4, 95% CI 0.98 – 2.0; $p = .060$) as cofactors, none affected freedom from endoleak.

Regarding TV patency, patients taking DAPT had higher patency rates (SAPT 93.4%, SE 0.7% vs. DAPT 97.0%, SE 0.6%; log rank $p = .007$) at thirty six months (Fig. 2). After performing Cox regression analysis for COPD (HR 1.05, 95% CI 0.69 – 1.61; $p = .79$), CHF (HR 1.1, 95% CI 0.6 – 2.0; $p = .78$), dyslipidaemia (HR 1.2, 95% CI 0.82 – 1.63; $p = .40$), sex (HR 1.1, 95% CI 0.74 – 1.76; $p = .55$), aortic dissection (HR 1.2, 95% CI 0.78 – 2.0; $p = .36$), presence of TAAA (HR 0.98, 95% CI 0.66 – 1.5; $p = .94$), and juxtarenal or pararenal aneurysm (HR 0.85, 95% CI 0.43 – 1.67; $p = .62$) as cofactors, none affected TV patency. However, B-EVAR was a predictor for worse TV patency (HR 2.03, 95% CI 1.36 – 3.03; $p < .001$). Stratifying patients by device configuration, DAPT was related to a higher patency rate within the B-EVAR (SAPT 87.2%, SE 2.1% vs. DAPT 94.9%, SE 1.9%; $p < .001$) and F-EVAR (SAPT 93.0%, SE 1.1% vs. DAPT 97.2%, SE 0.8%; $p = .020$) cohorts at thirty six months. Among 163 events of TV patency loss, 31.9% underwent a secondary intervention.

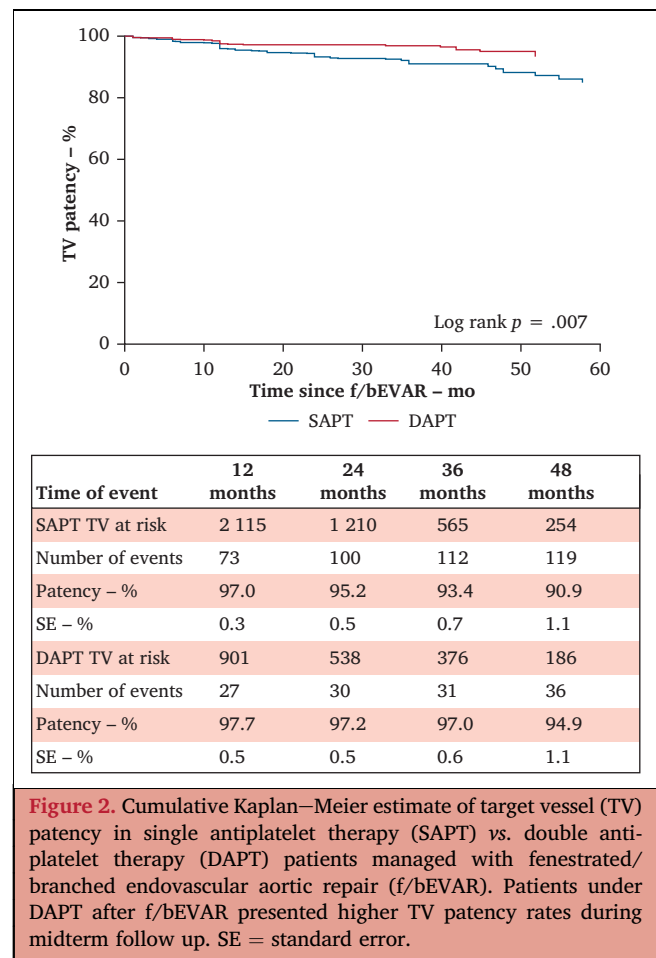
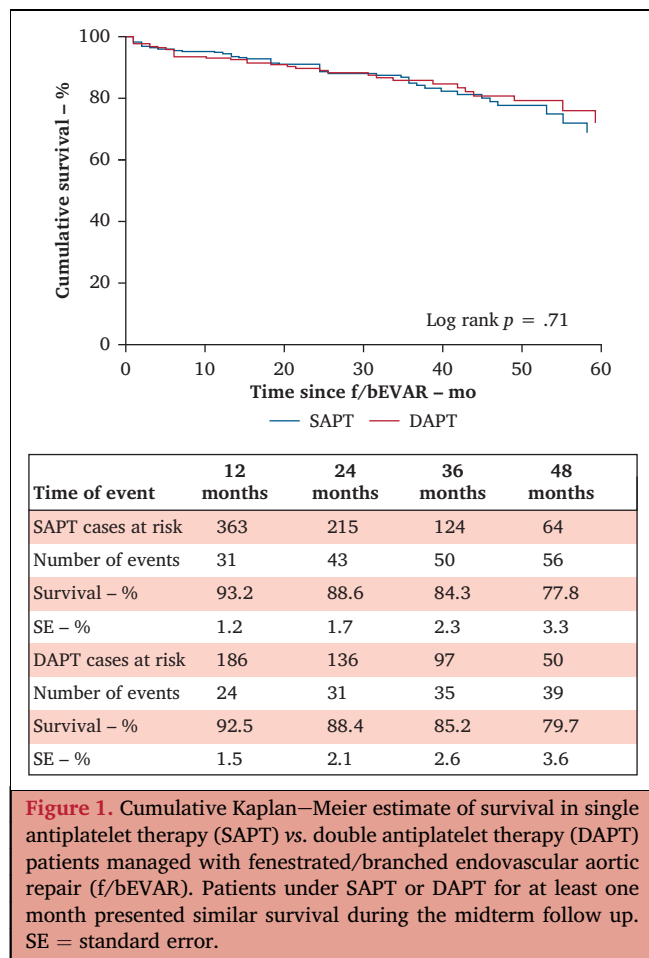
Subanalysis according to the duration of medication prescription

Patients with prescribed SAPT (540 patients) or DAPT (196 patients) for three to six months were analysed. No data on follow up haemorrhagic events were available. No statistically significant difference was detected in terms of thirty six month survival (SAPT 84.3%, SE 2.3% vs. DAPT 88.2%,

Table 3. Distribution of post-operative haemorrhagic adverse events at 30 days according to the post-operative antiplatelet treatment of single antiplatelet therapy (SAPT; $n = 955$) vs. double antiplatelet therapy (DAPT; $n = 475$) in patients managed with fenestrated and branched endovascular aortic repair.

Variable	SAPT ($n = 955$)	DAPT ($n = 475$)	p value	Multivariable analysis OR (95% CI)
ISTH defined major haemorrhagic events	72 (7.5)	30 (6.3)	.40	–
Intracranial haemorrhage	8 (0.8)	1 (0.2)	.16	–
Gastrointestinal haemorrhage	7 (0.7)	2 (0.4)	.48	–
Retroperitoneal haemorrhage	17 (1.8)	5 (1.1)	.29	–
Access site haemorrhagic events needing re-intervention	23 (2.4)	17 (3.6)	.21	–
Access site haemorrhagic events conservatively treated	43 (6.0)	10 (2.2)	.003	0.37 (0.18–0.76); $p = .007$

Data are shown as n (%). SAPT = single antiplatelet therapy; DAPT = double antiplatelet therapy; OR = odds ratio; CI = confidence interval; ISTH = International Society on Thrombosis and Haemostasis.



SE 2.9%; log rank $p = .19$) (Supplementary Fig. S2) or freedom from endoleak (SAPT 79.6%, SE 2.4% vs. DAPT 81.3%, SE 3.4%; log rank $p = .91$) (Supplementary Fig. S3). TV patency rates were higher in the DAPT group (SAPT 93.4%, SE 0.7% vs. DAPT 97.4%, SE 0.7%; log rank $p = .005$) (Supplementary Fig. S4).

Single antiplatelet therapy subanalysis

The SAPT cohort was divided into two groups: ASA (864 cases) and clopidogrel (91 cases). The comparative pre-operative characteristics are presented in Supplementary Table S3. Coronary artery disease and peripheral arterial disease were more common in the clopidogrel group (ASA 36.6% vs. clopidogrel 48.4%; $p = .027$; and ASA 16.7% vs. clopidogrel 33.0%; $p < .001$, respectively).

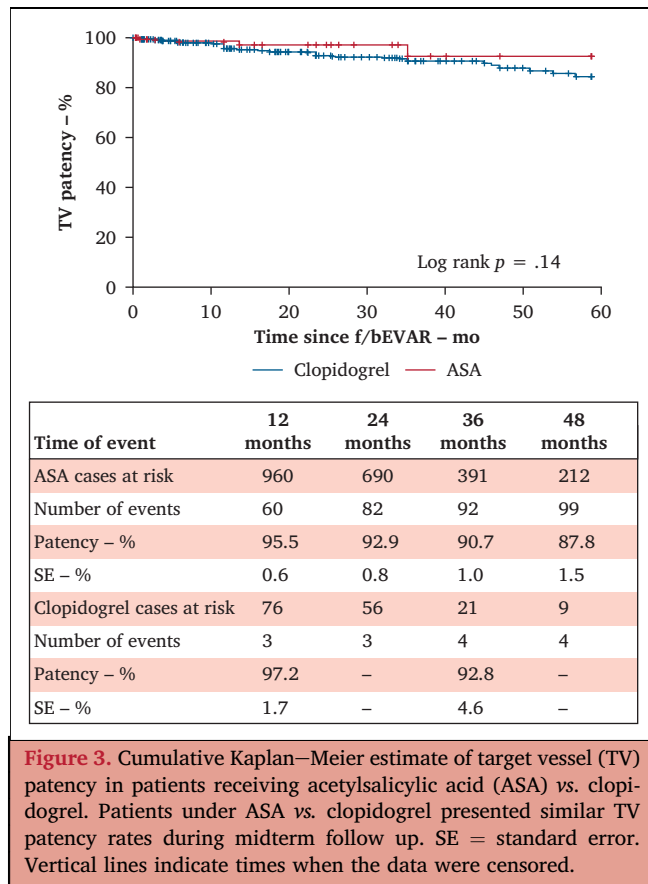
Regarding the 30 day outcomes, both groups performed similarly regarding death (ASA 2.0% vs. clopidogrel 3.3%; $p = .40$), cardiovascular events (ASA 11.8% vs. clopidogrel 13.2%; $p = .70$), and ISTH major haemorrhagic events (ASA 7.5% vs. clopidogrel 7.7%; $p = .95$). The comparative 30 day outcomes are presented in detail in Supplementary Table S4. No statistically significant difference was detected in follow up outcomes in terms of survival (ASA 84.8%, SE 2.3% vs. clopidogrel 78.6%, SE 9.1%; log rank $p = .35$), freedom from endoleak (ASA 69.1%, SE 2.9% vs. 66.9%, SE 10.0%; log rank $p = .99$), freedom from type II endoleak

(ASA 79.8%, SE 2.5% vs. 74.6%, SE 9.9%; log rank $p = .85$), and TV patency (ASA 90.7%, SE 1.0% vs. clopidogrel 92.8%, SE 4.6%; log rank $p = .14$) (Fig. 3).

DISCUSSION

F/B-EVAR has been used more frequently during the last decade and currently comprises more than 50% of TAAA repairs.^{23,24} The lower peri-operative death and morbidity rates, especially among patients at higher surgical risk, have expanded the F/B-EVAR target population.^{24–28} However, re-interventions seem to be common during midterm follow up.^{28,29} The role of antithrombotic treatment, including the use of SAPT and DAPT, has not been evaluated in F/B-EVAR outcomes. This multicentre analysis with more than 1 400 patients suggested that DAPT performed better in early cardiovascular ischaemic event prevention, without an increase in haemorrhagic events, while its use was related to better TV patency during midterm follow up.

Current European Society for Vascular Surgery (ESVS) recommendations on the use of antithrombotic therapy for vascular diseases suggest the use of ASA (75 – 100 mg) in patients diagnosed with abdominal aortic aneurysms (Class IIb, level of evidence C).^{20,30} Regarding patients managed with complex endovascular repair, DAPT may be considered in the early post-operative period, in cases at risk of bridging stent occlusion (Class IIb, level of evidence C).³⁰ In



addition, the Delphi consensus on principles of optimal antithrombotic therapy and coagulation management during elective fenestrated and branched endovascular aortic repairs (PRINCE²SS) suggests the use of DAPT for one to six months after F/B-EVAR.¹² Nevertheless, the missing information in the literature on this topic are again acknowledged.¹²

Early death after F/B-EVAR has been estimated at 5% in elective cases, even for patients with extensive aortic disease.^{6,29,31} Post-operative cardiac complications, stroke, and SCI have been shown to affect the 30 day mortality rate after F/B-EVAR.^{31,32} In the current study, the lack of difference between SAPT and DAPT in these specific parameters, including the similar post-operative MI rates and the higher distribution of American Society of Anesthesiologists score (ASA score) IV patients within the DAPT group, potentially drove the equal early mortality rates between groups.^{29,32,33}

Cardiovascular ischaemic complications were lower among DAPT patients, mainly due to the significant differences in acute mesenteric and limb ischaemia events. While mesenteric ischaemia is a potentially fatal complication, acute limb ischaemia, which presents with a rate of 5% after endovascular aortic repair, does not affect early mortality but increases the need for re-intervention.^{34–36} Oral antiplatelet therapy in patients with various vascular diseases seems to be effective in preventing ischaemic vascular events.³⁷ Studies on potential combinations of antiplatelet drugs have shown encouraging results in terms of ischaemic

events in patients with peripheral arterial disease.^{37,38} However, the higher bleeding risk should be acknowledged, while the applicability of these findings in the F/B-EVAR population could be questioned.^{9,39}

Haemorrhagic events at 30 days were similar between groups, with an acceptable frequency. Patients with history of cancer as well as haematological and liver diseases were excluded, lowering *a priori* the risk of peri-operative haemorrhage in the current study.^{15–18} However, it should be mentioned, despite statistical significance not being reached, that DAPT patients had lower rates of ISTH major haemorrhagic events during the 30 day follow up. Surgeon and patient selection bias, administering DAPT in patients with lower haemorrhagic profile, and in cases with lower intra-operative bleeding loss or access complications should be considered when interpreting the findings of the current analysis. Previous data on patients taking DAPT needing endovascular aneurysm repair confirm that appropriate DAPT management peri-operatively does not increase the risk of early haemorrhagic complications.^{40,41} DAPT initiation using a window of 24 – 48 hours post-operatively is potentially good clinical practice, to prevent early haemorrhagic events after F/B-EVAR, especially in patients under cerebrospinal fluid drainage.

Different parameters have been investigated for TV outcomes, showing that TV adverse events are rather a multifactorial phenomenon.^{9–11} Regarding TV patency, the 30 day findings did not show any difference between groups. However, it should be mentioned that early TV occlusion is uncommon.^{29,42,43} When evaluating the impact of SAPT vs. DAPT on midterm TV patency, DAPT performed statistically significantly better, especially in B-EVAR cases.⁴⁴ The use of DAPT for three to six months also provided better outcomes on TV patency compared with one month DAPT administration. However, as data on bleeding events during follow up are missing, the use of DAPT for three to six months should be decided after individually evaluating the thrombotic and bleeding profile of each patient.

Clopidogrel resistance was not investigated in the current cohort, as it does not represent part of common clinical practice.⁴⁵ However, previous data have shown that in 4 – 30% of patients, clopidogrel does not achieve adequate platelet deactivation.⁴⁵ This fact may explain the worse outcomes in terms of major stroke within the clopidogrel group. In addition, the follow up outcomes, including survival, endoleak, and TV patency, were similar between patients taking ASA and clopidogrel. Resistance to clopidogrel is affected by external and genetic parameters, and no specific test is currently available.⁴⁵ The underpower of the clopidogrel subgroup, including 91 patients, and the lack of data on patient compliance should be acknowledged.

This study aimed to answer questions related to antiplatelet therapy after F/B-EVAR and to fill the gap in evidence among this cohort of patients. However, its retrospective design may have hampered robust recommendations. A future randomised controlled clinical trial could provide better quality of evidence regarding the best medical treatment after complex endovascular repair. The

findings of the current analysis indicate that conclusions regarding the use of SAPT vs. DAPT in other cardiovascular populations should not be directly applied in F/B-EVAR patients.

Limitations

The main limitation of this study was its retrospective nature. Patients managed during the last five years were selected as eligible to avoid the inclusion of cases managed during the learning curve of each centre; a factor that would be different between centres and could affect the findings. However, the exclusion of previously treated cases affected the sample size of the current analysis. Different pre- and post-operative surveillance protocols were used in the contributing centres. Anatomical and technical factors, including type of bridging stent and number of stents per TV, were not further analysed but represent a field needing further investigation. All patients were managed with the Cook platform to increase the homogeneity of the cohort and to decrease the already existing cofounders. Data reporting on the use of other devices as well as comparative analyses between the devices could potentially provide interesting findings. The effect of antiplatelet treatment in patients with previous cancer, haematological disorders, and liver disease was not investigated according to the study's protocol, as these patients are considered at high risk both for ischaemic and haemorrhagic events; however, these patients represent a field of interest for future evaluation. Patients managed with other types of antithrombotic treatment, including other antiplatelet agents and anticoagulants, were excluded by protocol to provide as safe outcomes as possible in terms of SAPT vs. DAPT comparative findings. These patients represent another cohort needing investigation, as the risks of thrombosis or embolisation and bleeding are different. The mean follow up was relatively short at twenty two months. Almost 35% of cases were excluded from follow up analyses due to lacking data on confirmed medication prescription. Patient compliance with medical treatment (daily consumption of the prescribed medication) could not be confirmed and its potential impact on follow up outcomes should be acknowledged. Data on adverse bleeding events during follow up were unavailable and the impact of extensive DAPT treatment could not be evaluated. The impact of the surgery itself on adverse events, including the use and number of closure devices, should be taken into consideration when evaluating the outcomes of the current analysis. Despite the fact that statistically DAPT was detected as an independent protector for acute mesenteric and limb ischaemia, surgical manoeuvres and decisions that may have led to adverse events cannot be excluded. Data on the management of acute mesenteric and limb ischaemia are unavailable.

Conclusions

DAPT was associated with better outcomes compared with SAPT in terms of cardiovascular ischaemic events after F/B-

EVAR, without an impact on major 30 day haemorrhagic events. Patients managed with DAPT for one to six months enjoyed better TV patency during midterm follow up.

CONFLICTS OF INTEREST

Nikolaos Tsilimparis is a proctor for Cook Medical and has intellectual property with Cook Medical and Bentley, receiving institutional fees. Stéphan Haulon is a consultant and has intellectual property with Cook Medical, GE Healthcare, and Bentley. Jonathan Sobocinski is a consultant for Cook Medical and receives grants and speaker fees from W L Gore. Enrico Gallitto is a clinical proctor for Cook medical F/B-EVAR. Nuno Dias is a consultant, proctor, and has intellectual property with Cook Medical. Wolf Eilenberg is a consultant and proctor for Cook Medical, receiving royalties, speaking fees, and research, travel, and educational grants. Kevin Mani is a consultant and receives grants from Cook Medical. Luca Bertoglio is a consultant and proctor for Cook Medical. Bijan Modarai is a consultant and proctor for Cook Medical. Florian Enzmann is a proctor for Cook Medical and receives speaker fees from Cook Medical and W L Gore. Mauro Gargiulo is a consultant and proctor for Cook Medical. Tilo Kölbel is a consultant and proctor for and has intellectual property with Cook Medical, receiving royalties, speaking fees, and research, travel, and educational grants. All authors declare no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work; and no other relationships or activities that could appear to have influenced the submitted work.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejvs.2024.09.030>.

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