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ORIGINAL PAPER

Incidence, predictors, and outcomes of DAPT disruption due to non-compliance vs. bleeding after PCI: insights from the PARIS Registry

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Abstract

Background The disruption of dual antiplatelet therapy (DAPT) due to non-compliance or bleeding is known to significantly increase the risk of adverse outcomes after percutaneous coronary intervention (PCI). However, it is currently unknown if there are differences in the predictors and clinical impact of disruption due to non-compliance compared with bleeding.

Methods The patterns of non-adherence to antiplatelet regimens in stented patients (PARIS) registry was an international, multicenter prospective study of PCI patients discharged on DAPT (aspirin + a $P2Y_{12}$ receptor). We analyzed the incidence, patient characteristics, predictors, and outcomes in patients with DAPT disruption due to non-compliance as compared to DAPT disruption due to bleeding in the PARIS registry. Predictors of non-recommended disruption and bleeding disruption were assessed using logistic regression. Risks associated with disruption on major adverse cardiac events (MACE, a composite of cardiac death, definite or probable stent thrombosis, spontaneous myocardial infarction, and target lesion revascularization) were analyzed using time-updated Cox regression over 2-year follow-up.

Results Out of 5018 patients, the rate of non-compliant DAPT disruption was 1.6% at 30 days ($n=79$), 6.5% at 12 months ($n=328$), and 9.1% at 2 years from PCI ($n=457$). The rate of bleeding DAPT disruption was 0.6% at 30 days ($n=32$), 3.1% at 12 months ($n=156$), and 4.6% at 2 years ($n=229$). Multivariate predictors of non-compliant disruption included female gender, history of smoking, acute coronary syndrome, and US patients which were associated with greater risk; and dyslipidemia and discharge PPI which were associated with lower risk. Multivariate predictors of bleeding disruption included older age, prior MI, and discharge warfarin which were associated with greater risk; and US region and intervention to the LAD which were associated with lower risk. Non-compliant disruption was associated with a significantly greater risk for MACE (HR 1.73, 95% CI 1.17–2.54, $p=0.006$) and spontaneous myocardial infarction (HR 2.93, 95% CI 1.85–4.65, $p<0.001$). Bleeding disruption was associated with a significantly greater risk for all-cause death (HR 1.93, 95% CI 1.22–3.08, $p=0.005$).

Conclusion Approximately 1 in 10 patients disrupts DAPT due to non-compliance and 1 in 20 disrupts DAPT due to bleeding. Disruption due to non-compliance resulted in higher risk for ischemic events and disruption due to bleeding had higher subsequent mortality. These data warrant efforts to focus on patient education in those at high risk of non-compliance.

Keywords DAPT · Disruption · Bleeding · Non-compliance · Ischemic

Introduction

The World Health Organization (WHO) reports that approximately 50% of patients do not take medications as prescribed, and that anywhere from one-third to two-third of hospitalizations are due to poor medication adherence, even in developed countries [1–3]. Additionally, a WHO medication adherence report noted that poor adherence increased costs by approximately $100 billion per year [4]. Unfortunately, patients with cardiovascular disease are particularly

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susceptible to non-adherence, in part due to the bleeding risk associated with antithrombotic therapy [5, 6]. In patients undergoing PCI, adherence to dual antiplatelet therapy (DAPT) is crucial to decrease the risk of ischemic events in patients with high cardiovascular risk [7], since aspirin and a P2Y12 inhibitor are necessary to prevent early thrombotic complications, such as stent thrombosis [8] after percutaneous coronary intervention (PCI) [9].

The PARIS registry [10] first investigated the effect of different modes of DAPT cessation, demonstrating that physician-recommended discontinuation was associated with lower MACE risk whereas disruption due to non-compliance or bleeding elevated risk for composite ischemic outcomes. Using the PARIS registry, this paper aims to specifically explore the incidence, characteristics, predictors, and outcomes of DAPT disruption due to non-compliance as compared to DAPT disruption due to bleeding, with the goal of better addressing the complex interrelationships between these DAPT cessation modes and subsequent cardiac risk.

Methods

Study design

The PARIS (Patterns of Non-Adherence to Antiplatelet Regimens in Stented Patients) registry is a prospective observational study of patients undergoing PCI with stent implantation in 15 clinical sites in the USA and Europe between July 1, 2009 and Dec 2, 2010. Adult patients (18 years of age or older) undergoing stent implantation in at least 1 native coronary artery and discharged on DAPT were eligible for enrollment. Prespecified categories for DAPT cessation included physician-recommended discontinuation, brief interruption (for surgery), or disruption (non-compliance or because of bleeding). All adverse events and episodes of DAPT cessation were independently adjudicated.

Objectives

The primary objectives of the PARIS study were to examine the different modes of DAPT cessation in patients with coronary artery disease undergoing PCI with stenting and to assess the associations between these modes and subsequent clinical events. In this study, we focused specifically on the disruption mode of cessation (either due to bleeding or non-compliance) and patients' baseline characteristics, predictors of disruption, and outcomes.

Definitions

DAPT cessation was classified as either discontinuation, interruption, or disruption. Discontinuation was defined as recommended, physician-directed withdrawal of DAPT. Interruption was defined as temporary cessation of antiplatelet medication due to surgical necessity that was reinstituted within 14 days. Disruption was defined as cessation of DAPT either due to bleeding or non-compliance. It should be noted that these classifications are not mutually exclusive, and that a patient could have had more than one mode of cessation during the course of the study. Cessation was further classified into brief (1–5 days), temporary (6–30 days), or permanent (> 30 days), and elective vs. urgent, and recommended vs. non-recommended.

Stent thrombosis was defined according to the ARC criteria [11]. Target lesion revascularization was defined as any repeat intervention of the target lesion or surgical bypass of the target vessel and further classified as clinically indicated or not clinically indicated. Death was classified as due to cardiac, vascular, or non-cardiovascular causes as specified by ARC criteria [11]. Spontaneous myocardial infarction was defined as the presence of clinical or electrocardiographic changes consistent with myocardial ischemia in the setting of increased cardiac biomarkers above the upper limit of normal in accordance with the universal definition [12]. Bleeding was classified with the Thrombolysis in Myocardial Infarction (TIMI), acute catheterization and urgent intervention triage strategy (ACUITY), and Bleeding Academic Research Consortium (BARC) criteria [13, 14].

Major adverse cardiovascular events (MACE) were defined as the composite of cardiac death, definite or probable stent thrombosis, spontaneous myocardial infarction, and clinically indicated target lesion revascularization.

Follow-up and event reporting

Follow-up was done via telephone by trained research coordinators at each participating site at 30 days, 6 months, 12 months, and 24 months. Source documents were obtained for those patients reporting any adverse events or any DAPT cessation. In cases of DAPT cessation, all patients were also asked to provide information about which drug (aspirin or a $P2Y_{12}$ inhibitor) was stopped, the dates of stopping and restarting, and the reasons that drug treatment was stopped (physician-direction, need for surgery, bleeding, other). An external Clinical Events Committee (CEC) adjudicated all adverse events and episodes of DAPT cessation.

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) and were compared using Student's *t* test. Categorical variables are presented as proportions and were compared using the χ^2 test. Multivariable logistic regression was used to identify predictors of disruption due to non-compliance or due to bleeding, using the on-DAPT

population as a reference. Logistic regression models using backward selection with $p < 0.1$ as entry and exit criteria were adjusted for the following variables: age, gender, dyslipidemia, hypertension, smoking history, prior myocardial infarction (MI), acute coronary syndrome (ACS), region (US vs. Europe), admission aspirin, thienopyridine, discharge warfarin, discharge proton pump inhibitor (PPI), and LAD intervention. Cox regression models using backward selection with $p < 0.1$ as entry and exit criteria were used to relate the baseline covariates and time-updated DAPT cessation (disruption due to bleeding vs. disruption due to non-compliance, with on-DAPT as reference group) to clinical outcomes. The following variables were included as candidate variables for the COX model: diabetes mellitus (DM), age, gender, region (US vs. Europe), stent type, chronic kidney disease (CKD), smoking history, education level, prior MI, prior PCI, prior CABG, bifurcation lesion, and any thrombosis.

Results

Of 5018 patients enrolled in the PARIS study, 111 disrupted at 30 days (2.2%), 484 at 12 months (9.6%), and 690 at 2 years (13.7%) (Fig. 1). Of these 690, 459 (66.5%) disrupted due to non-compliance, with 79 (11.4%) of them disrupting by 30-day follow-up, 328 (47.5%) by 12-month follow-up, and 459 (66.5%) by 2-year follow-up. Tables 1, 2 and 3 show the baseline characteristics, baseline medications, and procedural medications in the two groups, respectively.

As compared to non-compliant disruptors, patients who disrupted due to bleeding were older, weighed less, had higher prevalence of dyslipidemia and hypertension requiring medication, and higher prevalence of previous CAD (prior PCI, CABG, or MI) and prior CABG. As compared to other studies, PARIS had similar or slightly higher rates of non-adherence, although to our knowledge there has not yet been a study that used an identical definition of disruption to PARIS [15].

Figure 2 shows the multivariate predictors for disruption due to non-compliance and disruption due to bleeding. Women were significantly more likely to disrupt without recommendation [odds ratio (OR): 1.29, 95% confidence interval (CI): 1.04–1.60; $p = 0.0222$]. American patients were highly more likely to disrupt, odds ratio (OR): 6.13, 95% confidence interval (CI): 4.18–8.99; $p < 0.0001$], as were ACS patients [odds ratio (OR): 1.24, 95% confidence interval (CI): 1.00–1.53; $p = 0.0494$]. Patients who had a history of smoking were more likely to be non-compliant disruptors than were patients who had never smoked [odds ratio (OR): 1.23, 95% confidence interval (CI): 1.00–1.50; $p = 0.0453$]. Patients with dyslipidemia were significantly less likely to disrupt due to non-compliance [odds ratio (OR): 0.74, 95% confidence interval (CI): 0.58–0.95; $p = 0.0173$], as were patients discharged on PPI [odds ratio (OR): 0.65, 95% confidence interval (CI): 0.49–0.85; $p = 0.0018$].

Predictors associated with bleeding disruption were older age [odds ratio (OR): 1.05, 95% confidence interval (CI): 1.03–1.06; $p < 0.0001$], previous MI [odds ratio (OR): 1.81, 95% confidence interval (CI): 1.20–2.72; $p = 0.0047$], and discharge warfarin [odds ratio (OR): 2.46,

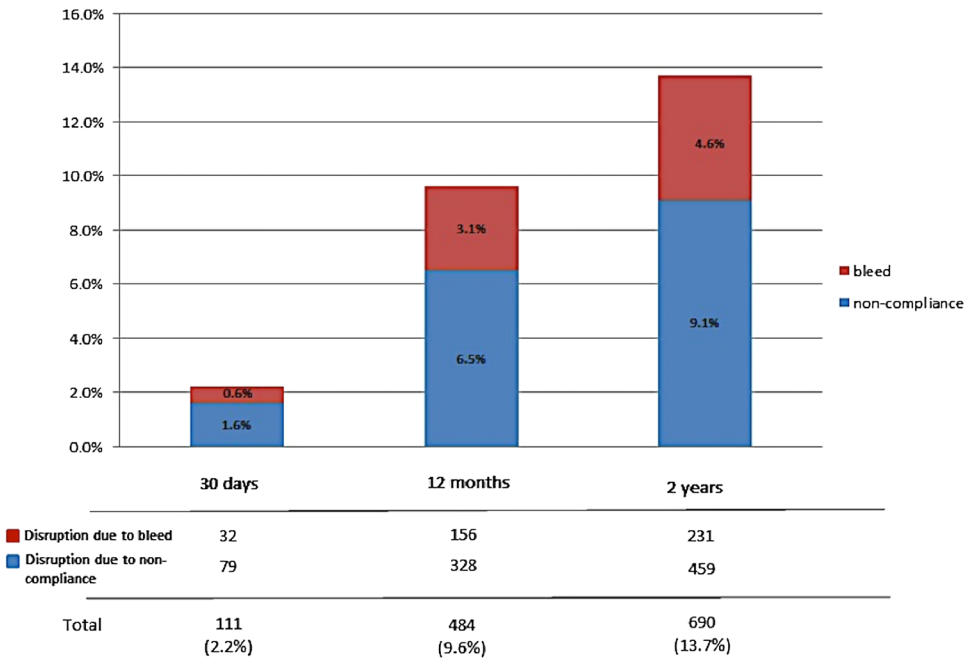

Fig. 1 Incidence of DAPT disruption in PARIS. Incidence of dual antiplatelet therapy disruption due to bleeding (red) vs. dual antiplatelet therapy disruption due to non-compliance (blue) reported at 30 days, 12 months, and 2 years post-PCI. *PARIS* patterns of non-adherence to antiplatelet regimens in stented patients, *DAPT* dual antiplatelet therapy

Table 1 Baseline characteristics

	Total ($N=690$)	Disruption non-compliance $N=459$ (67.0%)	Disruption due to bleeding $N=231$ (33.0%)	p value
Female gender	213 (30.9%)	140 (30.5%)	73 (31.6%)	0.77
Age (years), mean ± SD	(64.78 ± 12.28)	(62.59 ± 12.51)	(69.13 ± 10.54)	< 0.0001*
Height (cm), mean ± SD	(171.02 ± 10.20)	(171.02 ± 10.07)	(171.02 ± 10.47)	0.99
Weight (kg), mean ± SD	(85.83 ± 19.35)	(86.92 ± 19.72)	(83.68 ± 18.44)	0.04*
BMI (kg/m ^{2}), mean ± SD	(29.32 ± 6.17)	(29.73 ± 6.49)	(28.53 ± 5.43)	0.02*
Dyslipidemia requiring medication	489 (70.9%)	314 (68.4%)	175 (75.8%)	0.05*
Hypertension requiring medication	535 (77.5%)	341 (74.3%)	194 (84.0%)	0.004*
Family history of CAD	205 (29.7%)	148 (32.2%)	57 (24.7%)	0.04*
Ever smoker	394 (57.1%)	271 (59.0%)	123 (53.2%)	0.15
Current smoker	159 (23.0%)	117 (25.5%)	42 (18.2%)	0.17
Diabetes mellitus	219 (31.7%)	148 (32.2%)	71 (30.7%)	0.69
Insulin dependent	69(10.0%)	42 (9.2%)	27 (11.7%)	0.34
Education Level				0.22
Advanced university degree	53 (7.7%)	38 (8.3%)	15 (6.5%)	
Less than secondary	98 (14.2%)	59 (12.9%)	39 (16.9%)	
Missing	13 (1.9%)	11 (2.4%)	2 (0.9%)	
Secondary school	326 (47.2%)	210 (45.8%)	116 (50.2%)	
Tertiary university degree	200 (29.0%)	141 (30.7%)	59 (25.5%)	
Thienopyridine covered by insurance/subsidized by government				0.0006*
Missing	4 (0.6%)	3 (0.7%)	1 (0.4%)	
No	47 (6.8%)	42 (9.2%)	5 (2.2%)	
Yes	639 (92.6%)	414 (90.2%)	225 (97.4%)	
Ischemic history				
Previous MI	139 (20.1%)	77 (16.8%)	62 (26.8%)	0.002*
Previous PCI—balloon only	38 (5.5%)	23 (5.0%)	15 (6.5%)	0.42
Previous PCI—stent	235 (34.1%)	151 (32.9%)	84 (36.4%)	0.36
Previous CABG	75 (10.9%)	38 (8.3%)	37 (16.0%)	0.002*
Stroke (CVA)	25 (3.6%)	15 (3.3%)	10 (4.3%)	0.48
Transient ischemia attack	20 (2.9%)	13 (2.8%)	7 (3.0%)	0.88
Peripheral vascular disease	51 (7.4%)	33 (7.2%)	18 (7.8%)	0.78
Previous CAD (prior PCI, CABG, or MI)	318 (46.1%)	195 (42.5%)	123 (53.2%)	0.007*
Cardiac status at admission				
Silent ischemia	60(8.7%)	39 (8.6%)	21 (9.1%)	0.81
Stable angina	292(42.3%)	185 (40.3%)	107 (46.3%)	0.13
Acute coronary syndrome	338(49.0%)	235 (51.2%)	103 (44.6%)	0.10
Region				< 0.0001*
Europe	68(9.9%)	30 (6.5%)	38 (16.5%)	
U.S.	622(90.1%)	429 (93.5%)	193 (83.5%)	

Continuous variables are presented as mean ± standard deviation (SD) and were compared using Student's t test. Categorical variables are presented as proportions and were compared using the χ^2 test

MI myocardial infarction, *PCI* percutaneous coronary intervention, *CABG* coronary artery bypass graft, *CVA* cerebrovascular accident, *U.S.* United States

* Statistical significance with p value ≤ 0.05

95% confidence interval (CI): 1.43–4.21]; $p=0.0011$]. Additionally, patients who were from the US were less likely to disrupt medications due to bleeding [odds ratio (OR): 0.33, 95% confidence interval (CI): 0.19 to 0.57; $p=0<0.0001$), as were patients who had intervention to the left anterior descending coronary artery [LAD, odds ratio (OR): 0.65, 95% confidence interval (CI): 0.46–0.92; $p=0.0155$].

Table 2 Discharge medication

	Total ($N=690$)	Disruption not due to bleeding $N=459$ (67.0%)	Disruption due to bleeding $N=231$(33.0%)	p value
Discharge medications				
Aspirin	690 (100.0%)	459 (100.0%)	231 (100.0%)	
Thienopyridine	690 (100.0%)	459 (100.0%)	231 (100.0%)	
Thienopyridine type				0.67
Clopidogrel	642 (93.0%)	426 (92.8%)	216 (93.5%)	
Prasugrel	44 (6.4%)	31 (6.8%)	13 (5.6%)	
Ticlopidine	4 (0.6%)	2 (0.4%)	2 (0.9%)	
Anticoagulant	69 (10.0%)	30 (6.5%)	39 (16.9%)	< 0.0001*
Enoxaparin (LMWH)	3 (0.4%)	1 (0.2%)	2 (0.9%)	0.22
Warfarin	68 (9.9%)	30 (6.5%)	38 (16.5%)	< 0.0001*
Proton pump inhibitor	119 (17.2%)	67 (14.6%)	52 (22.5%)	0.009*

Continuous variables are presented as mean ± standard deviation (SD) and were compared using Student's t test. Categorical variables are presented as proportions and were compared using the χ^2 test

LMWH low molecular weight heparin

* Statistical significance with p value ≤ 0.05

Table 3 Procedural characteristics

	Total ($N=690$)	Disruption not due to bleeding $N=459$ (67.0%)	Disruption due to bleeding $N=231$ (33.0%)	p value
PCI vessel				
Left main, *n* (%)	26 (3.8%)	13 (2.8%)	13 (5.6%)	0.07
LAD, *n* (%)	309 (44.8%)	218 (47.5%)	91 (39.4%)	0.04*
Proximal LAD, *n* (%)	127 (18.4%)	92 (20.0%)	35 (15.2%)	0.12
LCx, *n* (%)	205 (29.7%)	133 (29.0%)	72 (31.2%)	0.55
RCA, *n* (%)	254 (36.8%)	163 (35.5%)	91 (39.4%)	0.32
Number of vessels treated				0.37
One	589 (85.4%)	394 (85.8%)	195 (84.4%)	
Two	98 (14.2%)	62 (13.5%)	36 (15.6%)	
Three	3 (0.4%)	3 (0.7%)	0 (0.0%)	
Bifurcation lesion, *n* (%)	93 (13.5%)	57 (12.4%)	36 (15.6%)	0.25
Chronic total occlusion, *n* (%)	24 (3.5%)	12 (2.6%)	12 (5.2%)	0.08
Thrombotic lesion, *n* (%)	56(8.1%)	41 (8.9%)	15 (6.5%)	0.27
Stent type				
Bare metal stent, *n* (%)	176 (25.5%)	107 (23.3%)	69 (29.9%)	0.06
DES 1st generation, *n* (%)	75 (10.9%)	58 (12.6%)	17 (7.4%)	0.04*
DES 2nd generation, *n* (%)	467 (67.7%)	316 (68.8%)	151 (65.4%)	0.36
Number of stents implanted				0.37
One	392 (56.8%)	260 (56.6%)	132 (57.1%)	
Two	197 (28.6%)	137 (29.8%)	60 (26.0%)	
More than two	101 (14.6%)	62 (13.5%)	39 (16.9%)	
Total stented length				0.88
≤ 20 mm	278 (40.3%)	184 (40.1%)	94 (40.7%)	
> 20 mm	412 (59.7%)	275 (59.9%)	137 (59.3%)	

Continuous variables are presented as mean ± standard deviation (SD) and were compared using Student's t test. Categorical variables are presented as proportions and were compared using the χ^2 test

LAD left anterior descending artery, *LCx* left circumflex, *RCA* right coronary artery, *DES* drug-eluting stent

* Statistical significance with p value ≤ 0.05

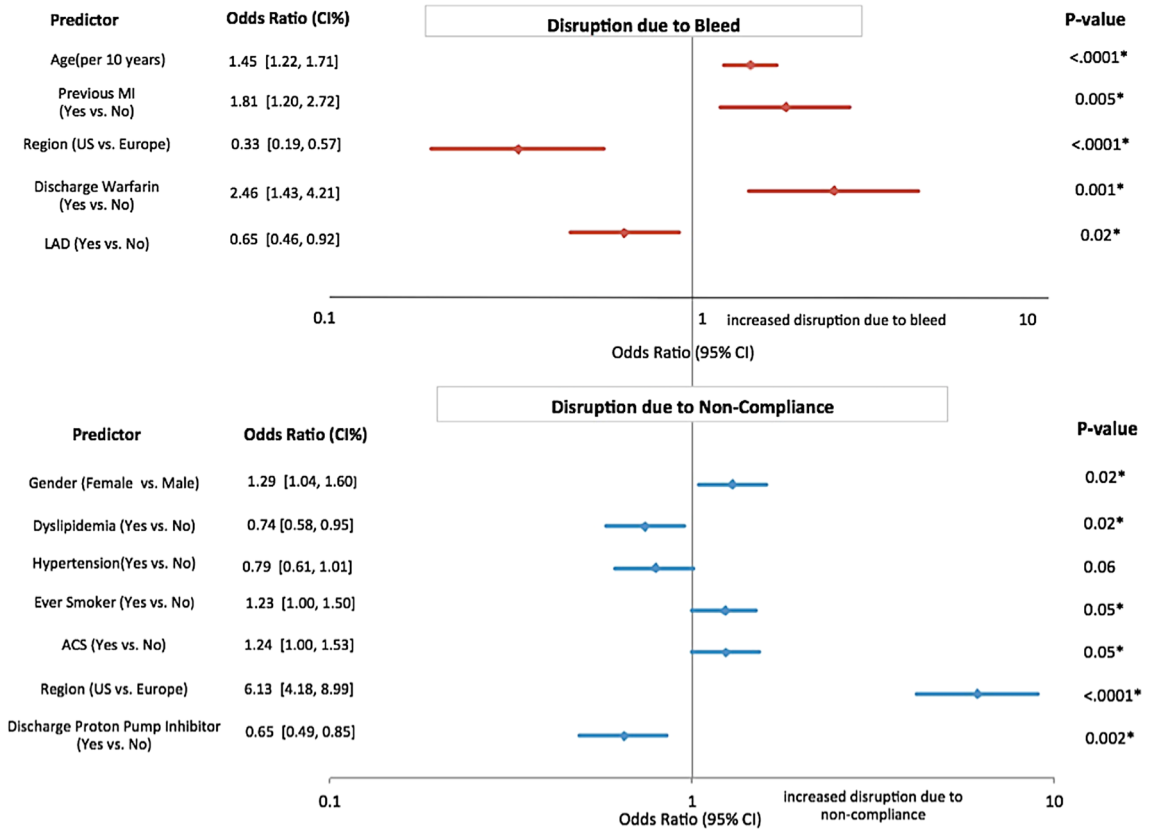

Fig. 2 Multivariate predictors of bleeding disruption and non-compliant disruption. Multivariable logistic regression was used to identify predictors of disruption due to non-compliance or due to bleeding, using the on-dual antiplatelet therapy population as a reference. Logistic regression models were applied using backward selection with $p < 0.1$ as entry and exit criterion. Error bars are 95% confidence intervals. *DAPT* dual antiplatelet therapy, *LAD* left anterior descending artery, *ACS* acute coronary syndrome, *MI* myocardial infarction, *PARIS* patterns of non-adherence to antiplatelet regimens in stented patients, *CI* confidence interval

Figure 3 shows the adjusted outcomes of DAPT disruption due to bleeding vs. the adjusted outcomes of disruption due to non-compliance. Patients who disrupted due to non-compliance had higher MACE rates [hazard ratio (HR): 1.73, 95% confidence interval (CI): 1.17–2.54; $p = 0.006$] and had a significantly higher rate of spontaneous MI [hazard ratio (HR): 2.93, 95% confidence interval (CI): 1.85–4.65; $p < 0.001$]. Patients who disrupted due to bleeding had a significantly higher rate of all-cause death [hazard ratio (HR): 1.93, 95% confidence interval (CI): 1.22–3.08; $p = 0.005$].

Discussion

The key findings of our analysis are as follows: 13.7% of patients disrupted DAPT over 2 years. Of these, 66.5% disrupted due to non-compliance and 33.5% due to bleeding. Patients who disrupted due to bleed tended to be older, to have hypertension or dyslipidemia requiring medication, to have had prior CABG or MI, and to weigh less than those who disrupted due to non-compliance. DAPT disruption due to bleeding led to higher rates of all-cause death whereas disruption due to non-compliance was associated with higher MACE and spontaneous MI. Additionally, the independent predictors of DAPT disruption illustrate the effect of demographic factors on non-compliance. Multivariate predictors of increased bleeding disruption included increased age, prior MI, and discharge warfarin; while multivariate predictors of increased non-compliant disruption included US region, female gender, smoking history, and ACS.

To our knowledge, the present analysis is the first study to compare characteristics and outcomes of patients who disrupt DAPT due to non-compliance vs. those who disrupt DAPT due to bleeding [14]. Consistent with previous studies, DAPT cessation due to non-compliance was associated with higher rates of subsequent thrombotic events following DES placement [16, 17]. The EDUCATE registry [18], a 2265 patient prospective observational study, also focused on non-adherence to DAPT, with non-adherence defined as missing ≥ 1 day of DAPT and severe non-adherence defined as missing ≥ 2 weeks. After 6 months, non-adherence

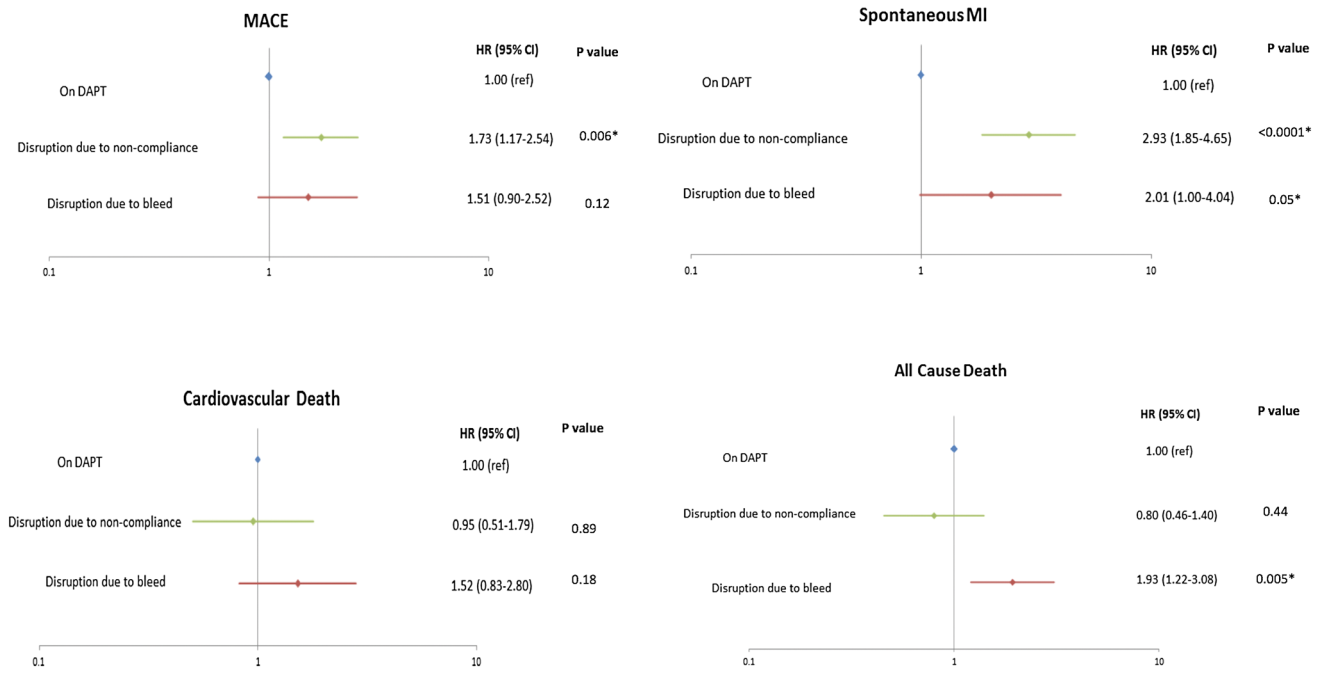

Fig. 3 Outcomes of DAPT disruption. Results of Cox model analyses for risk of MACE, spontaneous myocardial infarction (MI), cardiovascular death, and all-cause death. Boxes are hazard ratio point estimates and error bars are 95% confidence intervals. The following variables were included as candidate variables for the COX model: diabetes mellitus, age, gender, region (United States vs. Europe), stent type, chronic kidney disease, smoking history, education level, prior myocardial infarction, prior percutaneous coronary intervention, prior coronary artery bypass grafting, bifurcation lesion, and any thrombus. *DAPT* dual antiplatelet therapy, *MACE* a composite of cardiac death, definite or probable stent thrombosis, spontaneous myocardial infarction, and target lesion revascularization, *MI* myocardial infarction

occured in 9.6% of patients whereas severe non-adherence occured in 5.2%. These rates are comparable to the PARIS registry, with a rate of 9.6% disruption at 1 year. The only independent predictor for non-adherence in the EDUCATE registry, however, was bleeding. The current study revealed multiple independent predictors of disruption (i.e., age, gender, prior CAD, and discharge medication).

With additional knowledge on the predictors of non-compliance to DAPT, it is possible to identify and address specific patient populations at risk for disruption, and put them at lower risk for MACE and MI with DAPT adherence. As suggested by a white paper [19] on the importance of 12-month DAPT following DES placement, a greater effort should be made to educate patients on the reasons they are being prescribed $P2Y_{12}$ inhibitors, and the risks of medication cessation. Of note, our findings show that, of our measured metrics, region (US vs. Europe) is the strongest multivariate predictor for non-recommended DAPT disruption in the PARIS registry (OR = 6.13). This association might reflect differences in medication and insurance coverage between the US and Europe, particularly the lack of universal healthcare and greater out-of-pocket costs incurred by US patients. Thus, medical professionals and policy makers should be focused on ensuring patient access to obtaining their DAPT, in addition to education on the importance of the medication.

As the WHO suggests, the increased implementation of electronic health records can allow for better monitoring of patients who have not refilled their medications, and are thus likely non-adherent [20]. As has been seen in multiple clinical studies, medication adherence is particularly important in patients with existing cardiac conditions such as atrial fibrillation and diabetes [21, 22]. With this knowledge, it is necessary that patients, particularly those on antithrombotic medications, be contacted regarding their medication and actively followed up. It should also be noted that patients who have previous prescriptions are likely to have lower future adherence rates [23]. In a study by Benner et al., 6000 patients were monitored to see how adherence rates were affected by previous prescriptions when antihypertensive or lipid-lowering agents were added to their regimen. Adherence rates were 41%, 35%, and 30%, in patients who received 0, 1, and 2 previous medications, respectively [23]. These rates are especially alarming for patients with coronary artery disease, given many comorbidities leading to multiple medication prescriptions. Thus, it is particularly pressing to educate these patients on the importance of their CVD medications.

Limitations

PARIS is an observational study that precludes causal inferences and introduces the possibility of residual confounding on our risk estimates. Patients self-reported medication use, which introduces the possibility of recall or misclassification bias. More accurate methods of quantifying compliance such as measuring metabolites or pill counts were not performed in the PARIS registry. Toxicological analyses with measurements of platelet aggregation were not performed, which could lead to underreporting of any non-adherence. Additionally, non-DAPT drug cessation was not collected, which could have affected medication adherence and MACE outcomes. Lastly, we did not genotype patients for differing gene metabolites, which could influence the effectiveness of DAPT.

Conclusions

Approximately 1 in 10 patients disrupts DAPT due to non-compliance and 1 in 20 disrupts DAPT due to bleeding. Disruption due to non-compliance resulted in higher risk for ischemic events. These data warrant efforts to focus on patient education in subgroups at high risk of non-compliance.

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