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Sealing of Coronary Perforations With a Second-Generation Covered Stent Graft - Results From the PAST-PERF Registry

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ABSTRACT

Background: The PAST-PERF registry was initiated to collect data on the PK Papyrus covered stent, a second-generation device for the treatment of coronary artery perforations with enhanced mechanical properties, but with limited available data.
Methods: Patients treated for coronary artery perforations with the PK Papyrus stent at 14 international centers were retrospectively identified. The primary effectiveness outcome was successful sealing of the perforation. The primary safety outcome was a composite of all-cause mortality, definite or probable stent thrombosis, myocardial infarction and target lesion revascularization.
Results: Among the 94 included patients, 72.3% (68/94) had Ellis type III and cavity spilling perforations. Complete sealing was achieved in 93.6% ($n = 88$), and no sealing could be achieved in 3.2% ($n = 3$, including one patient with a geographical miss and one patient in whom the device could not be implanted). Pericardiocentesis was required in 25.0% ($n = 23$), emergency cardiac surgery was needed in 7.6% ($n = 7$), acute stent thrombosis was observed in 1.1% ($n = 1$), and in-hospital mortality occurred in 11.7% ($n = 11$). The median follow-up duration was 283 (IQR:40;670) days. At 6 and 12 months, the incidence of the primary safety endpoint was 26.6% [95%CI:18.6;37.1] and 32.0% [95%CI:22.8;43.4], mortality 15.0% [95%CI:9.0;24.6] and 19.0% [95%CI:11.3;30.0], and target lesion revascularization 5.5% [95%CI:2.0;14.6] and 7.7% [95%CI:3.1;18.2]. Two definite stent thrombosis occurred, one during the procedure and one on post-procedure day 233.
Conclusions: The registry demonstrates favorably high rates of successful stent delivery and sealing of coronary perforations using a second-generation covered stent with low target lesion revascularization and stent thrombosis rates.
Annotated table of content: The PAST-PERF registry demonstrates favorably high rates of successful stent delivery and sealing of coronary perforations using a second-generation covered stent with low target lesion revascularization and stent thrombosis rates. Specifically, complete sealing was achieved in 93.6% of patients ($n = 88/94$), and no sealing could be achieved in 3.2% ($n = 3$, including one patient with a geographical miss and one patient in whom the device could not be implanted). The 12-month mortality was 19.0% [95%CI:11.3;30.0], the rate of

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target lesion revascularization was 7.7% [95%CI:3.1;18.2], and two definite stent thromboses occurred (one during procedure and one on post-procedure day 233).
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1. Introduction

Coronary artery perforations (CAPs) are rare but potentially life-threatening complications that occur in approximately 0.3–0.5% of percutaneous coronary intervention (PCI) procedures [1–3]. Severe CAPs, such as Ellis grade III perforations (extravasation of blood through a frank [≥1 mm] perforation or spilling into an anatomic cavity), remain among the most dreaded complications for interventional cardiologists and require immediate action [4–6].

Placement of covered stents has become an alternative to surgery when other conservative approaches, such as prolonged balloon inflation or reversal of anticoagulation, fail [1,4]. Covered stents provide a physical barrier sealing the perforation, particularly for proximal CAPs, and have become the cornerstone of management for large-vessel perforations and indispensable tools in the cardiac catheterization laboratory [7,8].

Graftmaster® (Abbott Vascular, Santa Clara, CA, USA) was the first covered stent which became available in 1998 [9]. The basic limitation of this first-generation device is its bulky construction, with one membrane between two stainless-steel stents, impairing its deliverability, particularly through tortuous and calcified anatomies [9,10]. In contrast, PK Papyrus is a cobalt-chromium stent with thinner stent struts and a single stent layer design resulting in a lower crossing profile ranging from 1.18 to 1.55 mm and, consequently, leads to better trackability, deliverability and 5F compatibility [10]. Thus, it is also compatible with 6F guide catheter extensions which is handy in case of tortuous and calcified vessels.

Since its market launch in 2013, PK Papyurs has increasingly replaced the first-generation grafts. After approval in 2018, PK Papyrus also became available in the United States as the second approved covered stent for CAPs. To date, in-hospital data from two multicenter analyses are available, and one-year data from one single center analysis with 22 patients, and the SCAAR registry with 60 patients [9–12]. To collect further information about the medium-term safety and effectiveness of this device, the PAST-PERF (Papyrus Stentgraft for Sealing of Coronary Perforations) registry was initiated.

2. Materials and methods

2.1. Study design

PAST-PERF is an international, investigator-initiated, retrospective multicenter registry. Fourteen centres located in Germany, France, Poland, Sweden, Switzerland and South Africa provided their data. All patients in whom implantation of a PK Papyrus stent was attempted to treat peri-procedural CAPs were included. Data were collected during different time intervals, varying among the centers, from 2014 to 2019. The recorded data included baseline, procedural and in-hospital information and, as far as available, follow-up data. All centers confirmed that they provided all consecutive PK Papyrus cases and that they did not use any other covered stent for the treatment of CAPs during their individual enrollment period.

Ethic committee approval was obtained in each country. To avoid the exclusion of patients with lethal complications, and because the registry is truly observational, only completely anonymized data were collected to comply with data protection regulations (when possible, patient informed consent was collected). Accordingly, no on-site monitoring or event adjudication based on pseudonymized data could be conducted. Delivery of anonymized angiographic films was possible.

Data were captured using electronic case report forms provided by the Institut für Herzinfarktforschung in Ludwigshafen, transmitted using Secure Sockets Layer encryption with plausibility checks. Anonymized angiographic films, as far as available, were analyzed by two interventional cardiologists. In the case of divergent evaluations, a consensus meeting was arranged.

The registry was registered at the International Clinical Trials Registry Platform of the World Health Organization (DRKS00016956) and received a restricted grant from Biotronik AG, Buelach, Switzerland.

2.2. Device

The PK Papyrus covered stent system consists of a balloon-expandable covered single-layer stent mounted on a rapid-exchange delivery system. The stent body is made of cobalt-chromium and is the same as that used for the Orsiro drug-eluting stent (Biotronik AG, Buelach, Switzerland), with ultrathin struts of 60 μm (≥3.5 mm Ø 80 μm). The electrospun cover consists of non-woven, small fibres made of polyurethane, a biostable polymer. The device is available in diameters of 2.5, 3.0, 3.5, 4.0, 4.5, and 5.0 mm and lengths of 15, 20, and 26 mm. The maximum diameters for post-dilatation are 3.5 mm for small devices (2.5 and 3.0 mm stent diameter), 4.65 mm for medium devices (3.5 and 4.0 mm), and 5.63 mm for large devices (4.5 and 5.0 mm). The crossing profile of PK Papyrus is 1.25 mm for Ø 3.0 mm, and the delivery system is 5F compatible (≥Ø 4.5 mm 6F) (Fig. 1, Supplementary Table 1).

Fig. 1. PK Papyrus.

2.3. Outcomes and definitions

Perforations were classified according to the Ellis classification, as follows: type I: extraluminal crater without extravasation, type II: pericardial or myocardial blush without contrast jet extravasation, type III: extravasation through a frank (≥1 mm) perforation, cavity spilling: perforation into an anatomical cavity chamber, such as the coronary sinus. [5].

The primary efficacy outcome was the rate of successful sealing of CAPs, defined as no further leakage of contrast agent on the last angiography performed during the index procedure, irrespective of whether no, one or multiple stent-grafts were implanted. The Ellis type, the primary efficacy outcome, and all angiographic parameters were reassessed by the two interventional cardiologists mentioned above, who were aware of the operator's judgment.

The primary safety outcome was a composite of all-cause mortality, definite or probable stent thrombosis [13], myocardial infarction according to the universal and Society for Cardiovascular Angiography and Interventions (SCAI) definitions [14], and target lesion revascularization (TLR) [13] at the longest follow-up. The secondary endpoints were intra-procedural and post-procedural pericardiocentesis and rate of emergency cardiac surgeries. Peri-procedural myocardial infarctions were classified according to universal and SCAI definitions, and spontaneous myocardial infarction according to universal definitions [14,15].

2.4. Statistical analysis

Owing the descriptive nature of the registry, no formal sample-size calculation was performed. Quantitative variables were calculated as means and standard deviations (SDs) or medians and interquartile ranges (IQRs), and qualitative variables as numbers and frequencies. The analysis was based on avaialbe data. In case of missing core laboratory assessments, site data were used. The data of patients who died and those who survived were compared using the Pearson chi-square test or the Mann-Whitney-Wilcoxon test. Furthermore, 95% confidence intervals (CIs) and odds ratios (ORs) were calculated. The safety outcomes at follow-up are presented as frequencies and Kaplan-Meier curves. Kaplan-Meier curves for non-fatal events during the follow-up were generated using survival time of deceased patients as censored information. The analysis was conducted by the Stiftung Institut für Herzinfarktforschung using SAS statistical package version 9.4 (SAS, Cary, NC, USA).

3. Results

Implantation of PK-Papyrus for CAPs was attempted in 94 patients. The mean patient age was 72.8 ± 11.2 years, 24.5% ($n = 23$) of patients had diabetes, 39.4% ($n = 37$) had undergone previous PCIs, and 20.4% ($n = 19$) had a history of previous coronary artery bypass graft surgery (CABG) (Table 1).

Multivessel disease was present in 76.6% of patients ($n = 72$), moderate or heavy coronary calcification was observed in 90.4% ($n = 85$), and almost half of the perforated vessels (42.6%, $n = 40$) were in the left anterior descending artery. Ellis type III and cavity-spilling perforations were present in 68.1% ($n = 64$) and 4.3% (n = 4) of patients, respectively (Table 2).

The procedural characteristics are provided in Table 3. Complete sealing success was achieved in 93.6% ($n = 88$), and no sealing could be achieved in 3.2% ($n = 3$, including a patient with a geographical miss and a patient in whom the PK Papyrus could not be placed). The details of patients with post-procedure Thrombolysis in Myocardial Infarction (TIMI) flow <3 are provided in Supplementary Table 2.

During the procedure, 3 patients (3.2%) died, 7 (7.6%) required emergency cardiac surgery, 8 (9.2%) experienced peri-procedural myocardial infarctions, and one (1.1%) developed a definite stent thrombosis. The stent thrombosis occurred in a patient who presented with a type II perforation in a heavily calcified left anterior descending artery and received protamine during the procedure. After the procedure, 8 additional patients died, leading to an overall in-hospital mortality rate of 11.7% ($n = 11$), and one patient (1.1%) experienced a spontaneous myocardial infarction (Table 4). Of note, five patients with persisting shock who died peri-procedurally did not fulfil the biomarker-based definition of peri-procedural myocardial infarctions.

Table 1
Baseline characteristics.

	Total $N = 94$
Age [years]	72.8 ± 11.2
Male gender	71.0% (66/93)
Arterial hypertension	66.0% (62/94)
Diabetes mellitus	24.5% (23/94)
Insulin dependent	*43.5% (10/23)*
Previous MI	35.1% (33/94)
Previous PCI	39.4% (37/94)
Previous CABG	20.4% (19/93)
Smoking history	
Never smoked	51.6% (48/93)
Active smoker	18.3% (17/93)
Ex-smoker	30.1% (28/93)
Indication index procedure	
Stable angina	28.7% (27/94)
Unstable angina	10.6% (10/94)
NSTEMI	19.1% (18/94)
STEMI	18.1% (17/94)
Other	23.4% (22/94)

Displayed are percentages and numbers or mean ± standard deviation. CABG-coronary artery bypass grafting, MI-myocardial infarction, NSTEMI-non-ST-elevation myocardial infarction, PCI-percutaneous coronary intervention, STEMI-ST-elevation myocardial infarction.

Data beyond discharge are available for 86.2% of patients ($n = 81$), with a median follow-up of 283 days (IQR: 40;670) (Table 4). The incidence of the primary safety endpoint, a composite of all-cause mortality, definite or probable stent thrombosis, myocardial infarction and TLR, was 26.6% [95%CI:18.6;37.1] at 6 months and 32.0% [95%CI:22.8;43.4] at 12 months. The all-cause mortality rate was 15.0% [95%CI:9.0;24.6] and 19.0% [95%CI:11.3;30.0], and the TLR rate was 5.5% [95% CI:2.0;14.6] and 7.7% [95%CI:3.1;18.2] at 6 and 12 months, respectively (Fig. 2). One definite stent thrombosis beyond discharge occurred on post-procedure day 233 in a patient who presented after preceding PCI for non-ST-segment elevation myocardial infarction in a non-calcified left anterior descending artery.

Of the 12 patients with side-branch perforations, 3 experienced complications. In one of these 3 patients, the device could not be delivered as the perforation was too distal, one patient required emergency surgery, and one patient died. Complete sealing after PK-Papyrus implantation was achieved in the latter two patients.

Patients who died were significantly older at baseline (77.9 ± 12.2 years versus 71.6 ± 10.6 years, $p = 0.042$) and had a significantly lower post-procedural TIMI flow (TIMI flow 3 in 72.2% versus 93.2%, $p = 0.013$) than patients who survived. Furthermore, with respect to procedural and in-hospital complications, patients who died had significantly more cardiac tamponades, pericardiocentesis, need for resuscitation, persistent shock at the end of the procedure, or persistent occlusion of a major side branch; however no such relationship were observed for post-discharge complications (Supplementary Tables 3–6). The details of patients who died (including considerations in terms of stent thrombosis) and those who had emergency cardiac surgery are provided in Supplementary Tables 7 and 8, respectively.

At discharge, 21.7% ($n = 18$) were on anticoagulation therapy (for not stent-graft-related indications, predominantly for atrial fibrillation, in all but one case). The recommended antiplatelet therapy beyond discharge included acetylsalicylic acid in 96.4% ($n = 80$), clopidogrel in 75.9% ($n = 63$), ticagrelor in 16.9% ($n = 14$), and prasugrel in 3.6% ($n = 3$) of patients (Supplementary Table 9).

Table 2
Lesion characteristics.

	Total N = 94[a]
Extend of CAD	
LAD	80.9% (76/94)
RCA	67.0% (63/94)
RCX	59.6% (56/94)
Left main	18.1% (17/94)
Venous graft	11.7% (11/94)
Arterial graft	6.4% (6/94)
Multivessel CAD	76.6% (72/94)
Coronary calcification	
None	9.6% (9/94)
Moderate	50.0% (47/94)
Severe	40.4% (38/94)
Treated vessels	
LAD	50.0% (47/94)
RCA	31.9% (30/94)
RCX	21.3% (20/94)
Left main	10.6% (10/94)
Venous graft	8.5% (8/94)
Arterial graft	2.1% (2/94)
CTO	8.5% (8/94)
Perforated vessels	
LAD	42.6% (40/94)
RCA	28.7% (27/94)
RCX	16.0% (15/94)
Left main	5.3% (5/94)
Venous graft	7.4% (7/94)
Arterial graft	2.1% (2/94)
CTO	7.4% (7/94)
Perforation location	
Main branch	76.6% (72/94)
Side branch	12.8% (12/94)
Distal vessel	4.3% (4/94)
Graft/Anastomosis	8.5% (8/94)
Perforation type[b]	
Ellis type I	2.1% (2/94)
Ellis type II	25.5% (24/94)
Ellis type III	68.1% (64/94)
Ellis type III CS	4.3% (4/94)
Perforation mechanism	
Balloon	47.9% (45/94)
Wire	7.4% (7/94)
Stent	38.3% (36/94)
Scaffold	3.2% (3/94)
Rotablation	1.1% (1/94)
Other reasons	7.4% (7/94)

Displayed are percentages and numbers.
[a] Core laboratory data available in 79 patients.
[b] Type I: Extraluminal crater without extravasation, type II: pericardial or myocardial blush without contrast jet extravasation, type III: extravasation through frank (≥1 mm) perforation, type cavity spilling: perforation into an anatomic cavity chamber, coronary sinus, etc. CAD-coronary artery disease, CS-cavity spilling, CTO-chronic total occlusion, LAD-left anterior descending artery, RCA-right coronary artery, RCX-ramus circumflexus.

Table 3
Procedural characteristics.

	Total N = 94
Protamin administration	14.9% (14/94)
Papyrus implanted	
At perforation site	95.7% (89/93)
In main branch to cover SB perf.	3.2% (3/93)
At non-perforation site	1.1% (1/93)
# of Papyrus used, *N* = 93	1.3 ± 0.6
# of Papyrus used at perforation site, N = 88[a]	1.3 ± 0.5
1	78.4% (69/88)
2	19.3% (17/88)
3	1.1% (1/88)
4	1.1% (1/88)
Complete coverage of perforation with the first implanted stent-graft	88.2% (82/93)
Implanted stents at perforation site	
Stent 1, N = 88[a]	
Length, mm	20 ± 4
Diameter, mm	3 ± 2, N = 88
Pressure, atm	14 ± 3, N = 85
Stent 2, N = 19	
Length, mm	18 ± 3, *N* = 19
Diameter, mm	3 ± 1, N = 19
Pressure, atm	14 ± 3, N = 19
Sealing success[b]	
Complete	93.6% (88/94)
Immediate Sealing	*89.4% (84/94)*
Delayed Sealing	*4.3% (4/94)*
Partial	3.2% (3/94)
None	3.2% (3/94)
Complete sealing success for implanted devices	94.6% (84/93)
Post procedural TIMI flow	
TIMI 0	3.3% (3/92)
TIMI 1	4.3% (4/92)
TIMI 2	3.3% (3/92)
TIMI 3	89.1% (82/92)
Complete revascularization	
No	41.9% (39/93)
Yes	45.2% (42/93)
Partial (only CTO remains)	12.9% (12/93)

Displayed are percentages and numbers or mean ± standard deviation.
[a] Data missing on 5 stents.
[b] Core laboratory data available for 78 patients. CTO-chronic total occlusion, SB-side branch, TIMI-thrombolysis in myocardial infarction.

4. Discussion

To date, this is the largest series of PK Papyrus implantations for CAPs with 12-month follow-up data available, showing high stent delivery and sealing success rates, and low TLR and stent thrombosis rates considering the high-risk indication. Although only randomized data would bring ultimate clarity, it seems fair to say that first-generation covered stents have been superseded. The sandwich design with two layers of stainless-steel results in a thick crossing profile that limits deliverability and trackability, and also limits the use of the device in treating challenging coronary anatomies or more distal perforations [16]. In contrast, PK Papyrus, with its ultrathin stent struts and thin highly elastic polyurethane membrane, rather behaves like a conventional modern stent and can also access more distal lesions [7]. Likewise, a recent editorial recommended that new-generation covered stents should be used for better deliverability and possibly lower thrombogenicity, stating that covered stents in general are important treatment modalities for this indication, despite the high complication rates [17].

4.1. Comparison with other devices

PK Papyrus has a lower profile than Graftmaster and the Over and Under respective AneuGraft pericardium-covered stents (Amnis Therapeutics, Or Akiva, Israel). Its profile is similar to that of the BeGraft stent (Bentley InnoMed GmbH, Hechingen, Germany), which is also 5F compatible (Supplementary Table 1) [9,16]. In practice, this results in improved delivery. In our series, the device was successfully delivered in 98.9% of cases. Likewise, in a two-center analysis, PK Papyrus was successfully delivered in all cases, whereas delivery was not possible in 10% of patients in the Graftmaster group [11]. In SCAAR, a successful procedure was achieved in 83.8% for Graftmaster, 83.3% for Over and Under, 85.2% for AneuGraft, and 91.7% for PK Papyrus [9]. Furthermore, the time to delivery was nearly half of that for Graftmaster (8 ± 11 min versus 15 ± 16 min, $p = 0.001$) in the two-center analysis. Subsequently, the rates of pericardial effusion and cardiac arrest were significantly lower. These advantages were observed despite the longer stent

Table 4
Complications during the procedure, in-hospital, and at follow-up.

	Total N = 94
Procedure[a]	
Mortality	3.2% (3/94)
Pericardial tamponade	28.3% (26/92)
Pericardiocentesis	25.0% (23/92)
Definite stent thrombosis	1.1% (1/92)
Probable stent thrombosis	0.0% (0/92)
Resuscitation	9.8% (9/92)
Persisting shock at the end of procedure	6.5% (6/92)
Persisting occlusion of major side branch[b]	1.1% (1/92)
Emergency cardiac surgery	7.6% (7/92)
In-hospital (incl. procedure compl.)	
Mortality	11.7% (11/94)
Cardiovascular	*90.0% (9/10)*
Non-cardiac	*10.0% (1/10)*
Sudden death	0.0% (0/10)
Peri-procedural MI (SCAI def)	0.0% (0/87)
Peri-procedural MI (universal def.)	9.2% (8/87)
Spontaneous MI (universal def.)	1.1% (1/87)
Definite stent thrombosis	1.2% (1/85)
Probable stent thrombosis	0.0% (0/85)
Delayed hemodynamic instability	5.7% (5/87)
Pericardial tamponade	30.7% (27/88)
Emergency cardiac surgery	8.2% (7/85)
Resuscitation	13.8% (12/87)
Target Lesion Revascularisation	3.4% (3/87)
Target Vessel Revascularisation	2.3% (2/87)
Post discharge[c]	
Mortality (excluding hospital death)	8.6% (7/81)
Spontaneous MI (universal def.)	0.0% (0/81)
Definite stent thrombosis	1.2% (1/81)
Probable stent thrombosis	0.0% (0/81)
Delayed hemodynamic instability	1.2% (1/81)
Delayed pericardial tamponade	0.0% (0/81)
Delayed insertion of pericardial drain	0.0% (0/81)
Emergency cardiac surgery	0.0% (0/81)
Resuscitation	1.2% (1/81)
Target Lesion Revascularisation	6.2% (5/81)
Target Vessel Revascularisation	4.9% (4/81)
Non-Target Vessel Revascularisation	8.6% (7/81)

Displayed are percentages and numbers.
[a] Procedure events include events that occurred in the catheterization laboratory.
[b] Due to stent-graft (=2.0 mm).
[c] Median follow-up 283 days (40,670). MI-myocardial infarction.

length (20 ± 5 mm versus 16 ± 3 mm, $p < 0.001$) and near-significant higher calcification (82% versus 54%, $p = 0.051$) in the PK Papyrus group [11], supporting the assumption that single strut stents with a lower profile are more deliverable and may provide a more rapid and efficient management of CAPs [18]. Correspondingly, our sealing success rate was higher than that observed for Graftmaster, as shown in Supplementary Table 10 (93.6% versus 69–86.3%) [4,11].

In general, the comparison with other covered stents is limited by the retrospective single-arm design, the small number of patients in most studies, and the different indications included. However, as shown in Supplementary Table 10, which compares the outcomes of studies published within the last 2 years with the outcomes of PK Papyrus, the outcomes of our series well compare with those of other covered stents. At one year, the mortality rate was 19% compared with 12.7–41% for Graftmaster, and TLR occurred in 7.7% compared with 3–19.6%. Other devices such as Over and Under or AneuGraft have also shown outcomes within these ranges [3,9,11,19,20]. In theory, better trackability promotes deliverability, and the ultrathin strut profile that facilitates endothelialization shall result in fewer stent thromboses [17]. However, despite a trend toward less stent thrombosis with PK Papyrus (3.3%) compared with for Graftmaster (3.3–11.9%) [11,19], too little data are available to allow a judgment related to this rare complication.

A recent pooled analysis though reported increased stent thrombosis rates for first-generation polytetrafluroethylene (PTFE)-covered stents. This analysis included 29 studies, stratified for PTFE, PK Papyrus and pericardial stents, and found no difference in mortality or TLR; however stent thrombosis, pericardiocentesis, and emergency CABG were more frequent with PTFE stents, and in-stent restenosis was more frequent with pericardial stents [21].

4.2. Comparison with other outcomes of PK Papyrus

PK Papyrus was successfully delivered in all but one patient which is in agreement with delivery success rates of ≥95% reported in more than 300 patients across 4 analysis (Supplementary Table 9) [10–12].

Only two definite stent thrombosis occurred, one during the procedure (1.1%, 1/92, in a patient who received protamine) and one during the follow-up (1.2%, 1/81) (overall rate of 3.3% at 12 months according to Kaplan-Meier estimation). Although these outcomes are in line with 2 other analyses [10,11], the SOS-registry reported an in-hospital stent thrombosis rate of 8% [12]. As the SOS-registry has only been presented at the Transcatheter Cardiovascular Therapeutics 2019 conference and has not yet been published, the reason for this unexpected difference has not been provided thus far. The population consists of a mix of CAPs and off-label indications, and the definition of stent thrombosis and periprocedural anticoagulation therapy was unclear. Notably, the emergency setting of CAPs with heparin reversal, discontinuation of dual antiplatelet therapy (DAPT), and pericardial effusion with subsequent pericardial inflammation can trigger platelet aggregation. Currently, controversy exists about the possibility that protamine may cause more harm than good in large coronary perforations, as it promotes the risk of coronary thrombosis [4,17].

4.3. Baseline and procedural characteristics in association with clinical outcomes

Owing the emergency indication, the mortality of CAPs is higher than that in conventional PCI [7]. The identified predictors for 30-day mortality were age, diabetes, previous myocardial infarction, renal disease, ventilator support, circulatory support, glycoprotein inhibitor use, pericardial tamponade, and stent type [2,22]. Likewise, in our series, we found that patients who died were older (one-third of patients who died were aged ≥85 years), and had more frequent pericardial tamponade, pericardiocentesis, resuscitations, shock, and persistent occlusion of a major side branch. Furthermore, we found a trend toward a higher mortality rate in patients who received protamine: 27.8% (5/18) of patients who died received protamine whereas 11.8% (9/76) of patients who survived received protamine (OR 2.86 [95%CI:0.83–9.94], $p = 0.088$).

All 7 patients who required emergency cardiac surgery had moderate or severe calcification and Ellis type III or cavity-spilling perforations at baseline. Interestingly, surgery was needed despite complete sealing in 4 patients (Supplementary Table 8).

5. Limitations

The main limitation of this study was the small number of patients. Furthermore, the retrospective design precluded a direct comparison with other devices. However, owing the rare occurrence and emergency status of CAPs and the associated life-threatening situation, prospective evaluations are not feasible. Thereby, the study needs to rely on data that at least show the safety and efficacy of the device. Furthermore, full anonymization was required, preventing source document verification, query resolution or event adjudication, potentially leading to underreporting of events. Nevertheless, as far as possible, utmost efforts were made to obtain reliable data, such as through core laboratory assessments of anonymized angiographic films. Post-procedural biomarkers were not systematically assessed, potentially obscuring the

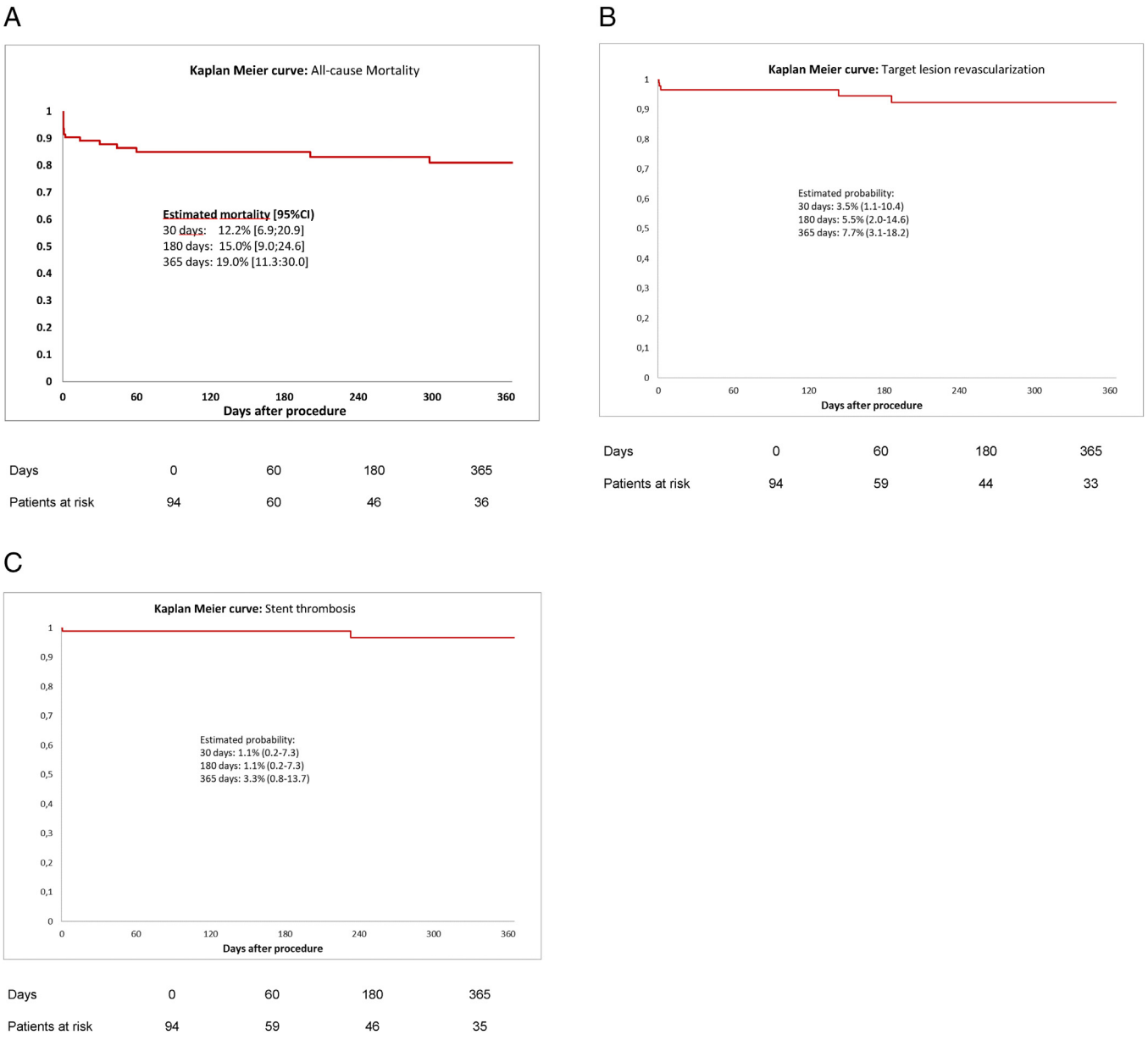

Fig. 2. Kaplan-Meier estimates of all-cause mortality, target lesion revascularization and definite or probable stent thrombosis.

occurrence of post-procedural myocardial infarction. The accurate estimation of the magnitude of peri-procedural myocardial infarctions according to biomarker-based definitions was further challenged by the significant number of patients dying during or early after the intervention due to persisting shock.

Another major limitation is the lack of intravascular imaging, which would have been of interest as the thinner struts of PK Papyrus and the associated better deliverability could theoretically result in a lower risk of malapposition and earlier endothelial coverage, and ultimately in a reduced thrombotic risk compared with first-generation two-layered PTFE-coated devices. Furthermore, reliable follow-up data for DAPT usage are missing in our series; however at least it was evident that DAPT was planned for 12 months in most of the cases, as recommended in the literature [16].

Although long-term outcomes are missing, the median follow-up is at least beyond the estimated time of complete endothelialization at 178 days, as demonstrated in an animal model (data on file at Biotronik).

6. Conclusions

This registry demonstrated excellent stent delivery success and good sealing of coronary artery perforations using a second-generation single-layer covered stent, with low TLR and stent thrombosis rates, providing further evidence on the ease of use, safety and efficacy of this device. However, the in-hospital mortality rate remains high in this group of patients.

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Conflict of interest statement

Ralf Birkemeyer reports grants and non-financial support from Biotronik during the conduct of the study; and personal fees and non-

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CRediT authorship contribution statement

Birkemeyer: Conceptualization, data curation, formal analysis, funding acquisition, investigation, methology, project administration, writing, review & editing.

Olivecrona, Hellig, Wöhrle, Rottbauer, Witkowski, Kuliczkowski, Bernhardt, Bettels, Schrage, von zur Mühlen, Cook, Miljak, Eggbrecht, Eric Eeckhout, Westermann, Monsegu, Dumonteil: investigation, review & editing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.carrev.2020.10.012.

References

[1] Shimony A, Joseph L, Mottillo S, Eisenberg MJ. Coronary artery perforation during percutaneous coronary intervention: a systematic review and meta-analysis. Can J Cardiol. 2011;27:843–50.
[2] Kinnaird T, Kwok CS, Kontopantelis E, Ossei-Gerning N, Ludman P, de Belder M, et al. Incidence, determinants, and outcomes of coronary perforation during percutaneous coronary intervention in the United Kingdom between 2006 and 2013: an analysis of 527 121 cases from the British Cardiovascular Intervention Society database. Circ Cardiovasc Interv 2016; 9. pii: e003449. doi: https://doi.org/10.1161/CIRCINTERVENTIONS.115.003449.
[3] Shaukat A, Tajti P, Sandoval Y, Stanberry L, Garberich R, Nicholas Burke M, et al. Incidence, predictors, management and outcomes of coronary perforations. Catheter Cardiovasc Interv. 2019;93:48–56.
[4] Pavani M, Cerrato E, Latib A, Ryan N, Calcagno S, Rolfo C, et al. Acute and long-term outcomes after polytetrafluoroethylene or pericardium covered stenting for grade 3 coronary artery perforations: insights from G3-CAP registry. Catheter Cardiovasc Interv. 2018;92:1247–55.
[5] Ellis SG, Ajluni S, Arnold AZ, Popma JJ, Bittl JA, Eigler NL, et al. Increased coronary perforation in the new device era. Incidence, classification, management, and outcome. Circulation. 1994;90:2725–30.
[6] Eeckhout E, De Palma R. Coronary perforation: an inconvenient complication. JACC Cardiovasc Interv. 2011;4:96–7.
[7] Xenogiannis I, Brilakis ES. Advances in the treatment of coronary perforations. Catheter Cardiovasc Interv. 2019;93:921–2.
[8] Patel NJ, Heuser RR. Covered stents: a 25-year odyssey. Catheter Cardiovasc Interv. 2019;93:E189–90.
[9] Harnek J, James SK, Lagerqvist B. Very long-term outcome of coronary covered stents: a report from the SCAAR registry. EuroIntervention. 2019;14:1660–7.
[10] Kandzari DE, Birkemeyer R. PK papyrus covered stent: device description and early experience for the treatment of coronary artery perforations. Catheter Cardiovasc Interv. 2019;94:564–8.
[11] Hernandez-Enriquez M, Lairez O, Campelo-Parada F, Lhermusier T, Bouisset F, Roncalli J, et al. Outcomes after use of covered stents to treat coronary artery perforations. Comparison of old and new-generation covered stents. J Interv Cardiol. 2018;31:617–23.
[12] Hernandez-Enriquez M. SOS PK Papyrus, an observational study of patietns with covered PK Papyrus stent. Presented at TCT 19; Sep 27,2019; San Francisco, CA.
[13] Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, et al. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation. 2007;115:2344–51.
[14] Moussa ID, Klein LW, Shah B, Mehran R, Mack MJ, Brilakis ES, et al. Consideration of a new definition of clinically relevant myocardial infarction after coronary revascularization: an expert consensus document from the Society for Cardiovascular Angiography and Interventions (SCAI). J Am Coll Cardiol. 2013;62:1563–70.
[15] Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. Circulation. 2012;126:2020–35.
[16] Kufner S, Schacher N, Ferenc M, Schlundt C, Hoppmann P, Abdel-Wahab M, et al. Outcome after new generation single-layer polytetrafluoroethylene-covered stent implantation for the treatment of coronary artery perforation. Catheter Cardiovasc Interv. 2019;93:912–20.
[17] Colombo A, Mangieri A. Should we implant a covered stent only when there is no other solution? EuroIntervention. 2019;14:1626–7.
[18] Seth A, Singh VP. Polytetrafluoroethylene covered stents during PCI: wanting more from our "savior". Catheter Cardiovasc Interv. 2019;94:562–3.
[19] Hachinohe D, Latib A, Laricchia A, Iannopollo G, Demir OM, Ancona MB, et al. Long-term follow-up of covered stent implantation for various coronary artery diseases. Catheter Cardiovasc Interv. 2019;94:571–7.
[20] Parikh P, Banerjee K, Sammour Y, Ali AF, Sankaramangalam K, Nair R, et al. Utilization and outcomes of polytetrafluoroethylene covered stents in patients with coronary artery perforation and coronary artery aneurysm: single center 15-year experience. Catheter Cardiovasc Interv. 2019;94:555–61.
[21] Nagaraja V, Schwarz K, Moss S, Kwok CS, Gunning M. Outcomes of patients who undergo percutaneous coronary intervention with covered stents for coronary perforation: a systematic review and pooled analysis of data. Catheter Cardiovasc Interv. 2019. https://doi.org/10.1002/ccd.28646 [Epub ahead of print].
[22] Lee WC, Hsueh SK, Fang CY, Wu CJ, Hang CL, Fang HY. Clinical outcomes following covered stent for the treatment of coronary artery perforation. J Interv Cardiol. 2016;29:569–75.