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REVIEW

Drug-Coated Balloon-Only Percutaneous Coronary Intervention for the Treatment of De Novo Coronary Artery Disease: A Systematic Review

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ABSTRACT

Percutaneous coronary intervention (PCI) with a drug coated balloon (DCB) is a novel treatment which seeks to acutely dilate a coronary stenosis and deliver an anti-proliferative drug to the vessel wall (reducing the risk of re-stenosis), without implanting a drug eluting stent (DES). In this study, we performed a systematic review of stentless DCB-only angioplasty in de novo coronary artery disease. We identified 41 studies examining the effects of DCB-only PCI in a variety of clinical scenarios including small vessels, bifurcations, calcified lesions, and primary PCI. DCB-only PCI appears to be associated with comparable clinical outcomes to DESs and superior angiographic outcomes to plain-old balloon angioplasty. Although current data are promising, there is still a need for further long-term randomized control trial data comparing a DCB-only approach specifically against a second- or third-generation DES. A 4-week period of dual antiplatelet therapy provides a real advantage for the DCB-only PCI approach, which is not possible with most DESs. Since rates of adverse clinical outcomes are very low for all PCI procedures attention should be turned to the development of robust endpoints with which to compare DCB-only PCI approaches to the standard treatment with a DES.

Keywords: Coronary artery disease; De novo; Drug-coated balloon; Drug-eluting balloon; Percutaneous coronary intervention

Richard G. Bogle and Anne Burke-Gaffney are equally contributed.

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INTRODUCTION

Percutaneous coronary intervention (PCI) is the commonest procedure used in the invasive treatment of coronary artery disease (CAD) [1]. Historically, this has involved plain-old balloon angioplasty (POBA, limited by elastic recoil, dissection and restenosis) and the bare metal

stent (BMS, limited by in-stent restenosis/ISR and stent thrombosis/ST requiring the prophylactic use of dual anti-platelet therapy/DAPT) [2, 3]. Currently, the mainstay of coronary revascularization with PCI is with the drug-eluting stent (DES). This enables the local delivery of an anti-proliferative drug via a polymer and has a considerably lower incidence of ISR [4, 5]. The second- and third-generation DESs have further reduced the incidence of ISR and ST and are now preferred over first-generation devices [6]. However, DES use is still sub-optimal in small vessel disease (SVD); which occurs in 20–30% of patients with symptomatic CAD [7, 8]. Furthermore, there still remains a small but significant risk of ST. Late ST (> 30 days) and very late ST (> 12 months) have been especially problematic due to delayed stent endothelialization [9]. This necessitates the use of long-term prophylactic DAPT, which is associated with an increased risk of bleeding complications and mortality in the elderly as well as being an economic burden [10].

The drug-coated balloon (DCB) is a semi-compliant balloon coated with an anti-proliferative drug, which is rapidly released via an excipient upon inflation [11]. The vast majority of DCBs are coated with 3 μg/mm^2 of paclitaxel. The use of DCBs for the treatment of ISR has class Ia recommendation from the European Society of Cardiology [4]. However, their role in de novo coronary disease is still not clear. The DCB proposes certain advantages over the DES such as a reduced duration of DAPT and immediate homogenous drug release without the presence of a metal and polymer, which have been shown to provoke inflammatory reactions in vessels [12]. Table 1 summarizes the DCBs used in human de novo CAD studies that use DCB-only PCI. DCB-only PCI (also referred to as DCB-only angioplasty and the DCB-only approach) describes the inflation of a DCB (usually for 30–60 s) following acceptable pre-dilatation of a coronary lesion with a cutting/non-compliant balloon and where provisional/bailout stenting is reserved only in cases of an unsatisfactory result [13]. The 2013 German Consensus Group recommendations define this as residual stenosis > 30%; ≥ type C National Heart, Lung and Blood Institute (NHLBI) coronary dissection or a Thrombolysis In Myocardial Infarction (TIMI) flow < 3 [14]. This review aims to provide a comprehensive summary of the published data regarding the use of DCB-only PCI for the treatment of de novo CAD.

Table 1 Overview of the DCBs used in de novo DCB-only CAD studies

DCB name	Manufacturer	Excipient
Dior I	Eurocor (Bonn, Germany)	Dimethyl sulfate
Dior II	Eurocor (Bonn, Germany)	Shellac
Elutax SV	Aachen Resonance (Aachen, Germany)	Dextran
Restore	Cardionovum (Milan, Italy)	Shellac
Pantera Lux	Biotronik AG (Buelach, Switzerland, Germany)	Butyryl-tri-hexyl-citrate
IN.PACT Falcon	Medtronic-Invatec (Frauenfeld, Switzerland)	Urea
SeQuent Please	B. Braun Melsungen AG (Berlin, Germany)	Iopromide

DCB drug-coated balloon, *CAD* coronary artery disease

METHODS

This was a systematic review conducted in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. MEDLINE, EMBASE, and Cochrane databases were searched (see Appendix A in supplementary material). Included were randomized and observational human de novo CAD studies that employed a DCB-only approach, reporting a clinical outcome of any kind. Exclusion criteria included studies that only employed routine stenting and those that did not separately report results for de novo CAD lesions. This article is based on previously conducted studies and does not involve any new studies with human participants or animal subjects performed by any of the authors.

Preferred clinical outcomes were target lesion revascularization (TLR, defined as any repeat revascularization within the DCB/stented region, either clinically driven or due to > 50% restenosis at follow-up) and major adverse cardiovascular events (MACE, a composite outcome of all-cause mortality, TLR, and myocardial infarction/MI). There is some variability in the way studies define MACE and these have been highlighted (Appendix B in supplementary material). Angiographic data, where reported, were also extracted with the majority of studies reporting late luminal loss (LLL), measured in millimetres. This is defined as the vessel minimal luminal diameter (MLD) post-procedurally, subtracted from the MLD at follow-up. In studies that provided information on where the LLL was taken from, the in-balloon/stent LLL was preferred. Where only an in-segment LLL was reported, this was explicitly mentioned.

In studies that did not report these specific outcomes, other endpoints were instead extracted. Examples include: periprocedural MI (defined as 5 × the 99th percentile upper reference limit of normal for creatine kinase-myocardial band or troponin T, occurring within 48 h after PCI), target lesion thrombosis (TLT, an angiographic occlusion with an acute clinical presentation in a previously treated region), target vessel failure (TVF, a composite outcome of cardiac death, target vessel-related MI and TLR) and device-oriented adverse cardiovascular events (DOCE, a composite outcome of cardiac death, target vessel MI, stroke, and TLR). Other angiographic outcomes include: percentage diameter stenosis (%DS, defined as 100 multiplied by the difference between the reference vessel diameter/RVD and the MLD divided by the RVD), binary restenosis (defined as the presence of a %DS of ≥ 50%) and MLD post-procedure and at follow-up (where a LLL is not provided).

RESULTS

Databases were searched up to 13/03/2018 and identified 1535 results. Forty-one studies (reported over 43 publications) were included in the final review (Fig. 1). These either investigated the general use of DCB-only angioplasty or focused specifically on bifurcating lesions, primary PCI (PPCI, for acute coronary syndrome/ACS), calcified lesions or chronic total occlusions (CTOs). It should be noted that one paper, a registry of the MagicTouch (Concept Medicals Inc.) Sirolimus DCB, fulfilled the inclusion criteria but was not available at the time of writing this review.

PATIENT CHARACTERISTICS

As shown in Table 2, the majority of the 6586 patients enrolled in studies were male (82%) with a mean age of 65. Where registries report patient characteristics for both de novo CAD and ISR, this has been explicitly shown. Among the classical cardiovascular risk factors, hypertension and dyslipidemia were most frequently observed. Temporal inconsistencies existed between studies with regards to smoking habits. The mean percentage of diabetics seen was 37% although, overall, the PPCI studies showed a low prevalence of diabetic patients. The use of DCB-only PCI in de novo CAD was almost exclusively investigated in small vessels (< 2.8 mm). The exceptions to this cut-off value reported a mean vessel diameter (MVD) only marginally greater than 2.8 mm. The majority of studies report a %bailout stenting of below 25%, however certain studies do exceed this; reasons for this are later discussed.

DCB-Only Angioplasty in General De Novo CAD

The use of DCB-only PCI in non-specific clinical scenarios, mainly in SVD, forms the main focus of the current literature. Full details of all study outcomes are provided in Table 3.

DCB vs. DES

PICCOLETO compared the Dior I DCB to the 1st-generation DES, Taxus Liberté [15]. It was stopped prematurely due to clear superiority of the DES. However, certain factors explain these

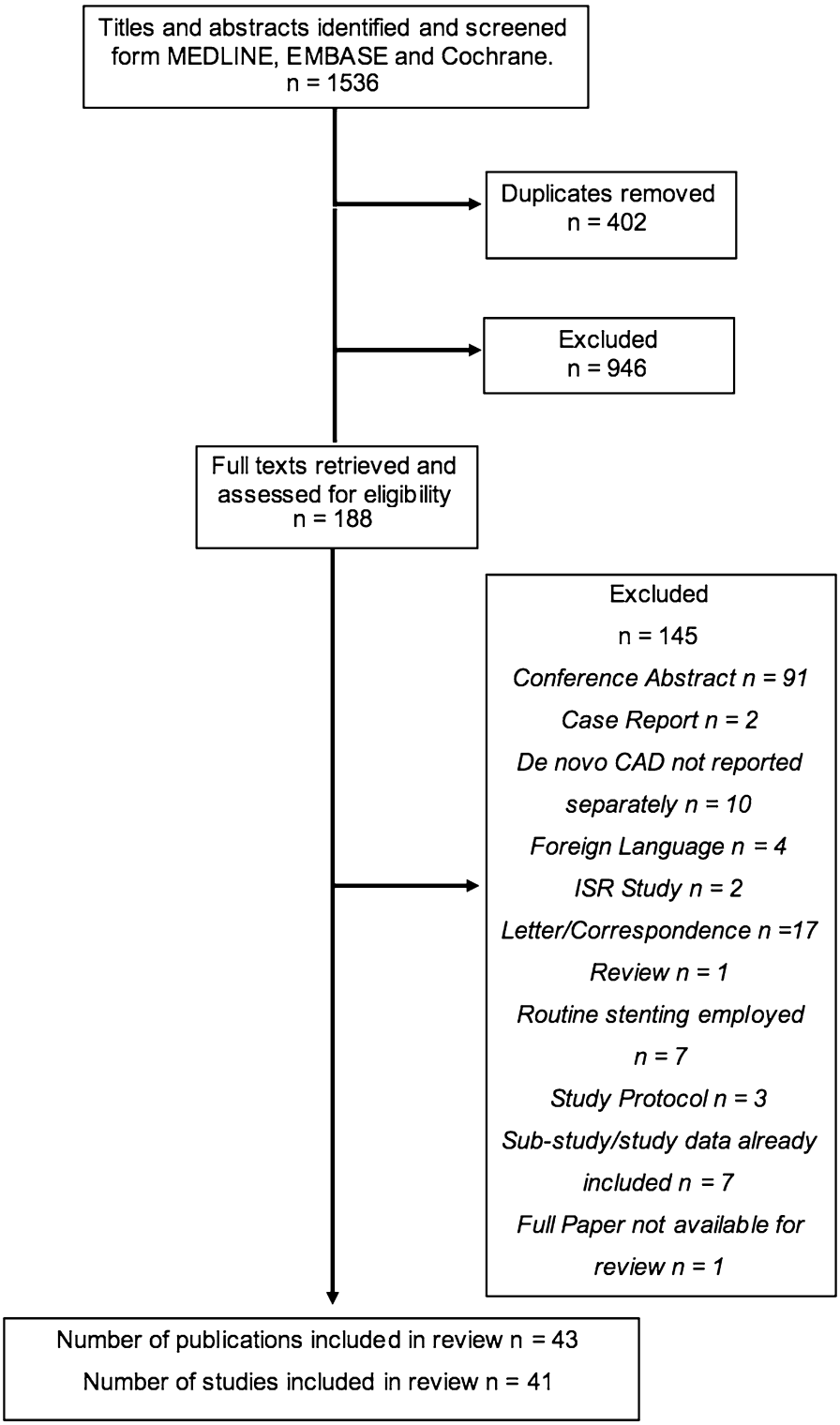

Fig. 1 PRISMA flowchart outlining the study selection process from the initial search download to title and abstract screening to full text analysis. Reasons for removal of full texts are provided

Table 2 Summary of the patient characteristics of studies investigating the use of DCBs alone in de novo coronary artery disease

Author	Number of patients	Mean vessel diameter (mm)	Bail out (%)	Mean age	Male *N* (%)	Diabetes *N* (%)	Smokers *N* (%)	HTN *N* (%)	Dyslip. *N* (%)
General de novo lesions—randomised studies									
Cortese et al. (2010) [15]	60 (29 DCB, 31 DES)	2.54 (DCB), 2.58 (DES)	36%	67	44 (73%)	24 (42%)	NR	41 (72%)	30 (53%)
Latib et al. (2012, 2015) [19, 20]	182 (90 DCB, 92 DES)	2.15 (DCB), 2.25 (DES)	20%	65	143 (79%)	74 (41%)	25 (14%)	147 (81%)	144 (79%)
Nishiyama et al. (2016) [23]	60 (DCB 27, DES 33)	2.88 (DCB), 2.72 (DES)	0%*	69	44 (73%)	25 (42%)	36 (60%)	50 (83%)	47 (78%)
Funatsu et al. (2017) [28]	133 (DCB 92, POBA 41)	2.04 (DCB), 1.99 (POBA)	3%	68	100 (75%)	57 (43%)	NR	107 (80%)	104 (78%)
General de novo lesions—comparative observational studies									
Her et al. (2016) [29]	72 (DCB 49, POBA 23)	2.3 (DCB), 2.1 (POBA)	0%*	63	49 (68%)	25 (35%)	21 (29%)	45 (63%)	43 (60%)
Shin et al. (2016) [24]	66 (DCB 44, BMS/DES 22)	2.69 (DCB), 2.92 (DES/BMS)	0%*	60	50 (76%)	18 (27%)	25 (38%)	32 (48%)	27 (41%)
Sinaga et al. (2016) [25]	335 (172 DCB, 163 DES)	2.22 (DCB) vs. 2.44 (DES)	0%*	57	249 (74%)	168 (50%)	125 (37%)	238 (71%)	238 (71%)
Giannini et al. (2017) [22]	181 (90 DCB, 91 DES)	2.15 (DCB), DES NR (100% < 2.8)	20%	66	143 (79%)	76 (42%)	69 (38%)	146 (81%)	142 (78%)
Her et al. (2017) [27]	104 (DCB 52, DES 52)	2.3 (DCB), 2.2 (DES)	0%*	60	34 (33%)	44 (42%)	37 (36%)	60 (58%)	47 (45%)
Venetsanos et al. (2018) [26]	1648 (DCB 824, 824 DES)	NR (82% < 2.5)	8%	68	1724 (72%)	698 (29%)	NR	1588 (66%)	1413 (59%)

Table 2 continued

Author	Number of patients	Mean vessel diameter (mm)	Bail out (%)	Mean age	Male *N* (%)	Diabetes *N* (%)	Smokers *N* (%)	HTN *N* (%)	Dyslip. *N* (%)
General de novo lesions—observational studies									
Unverdorben et al. (2010, 2013) [17, 18]	118	2.35	27%	68	85 (72%)	51 (43%)	NR	103 (87%)	95 (80%)
Cuculi et al. (2012) [44]	79	2.8	5%	69	63 (80%)	19 (24%)	17 (21%)	56 (71%)	53 (67%)
Woehrle et al. (2012) [35]	491	2.56	21%	NR	379 (77%)	166 (34%)	192 (39%)	408 (83%)	348 (71%)
Calé et al. (2013) [40]	74 de novo (156 total)	NR (86% < 2.8)	3%	66	114 (73%)	68 (44%)	78 (50%)	129 (83%)	120 (77%)
Waksman et al. (2013) [47]	103	2.4	12%	63	82 (80%)	29 (28%)	37 (36%)	86 (84%)	61 (60%)
Basavarajah et al. (2014) [45]	79 de novo (184 total)	NR (70% < 2.5)	22%	66	160 (87%)	64 (35%)	99 (54%)	132 (72%)	130 (71%)
Toelg et al. (2014) [49]	105	2.5	23%	65	74 (71%)	38 (36%)	71 (68%)	81 (77%)	70 (67%)
Zeymer et al. (2014) [36]	447	2.14	6%	66	324 (73%)	164 (37%)	169 (38%)	360 (80%)	308 (69%)
Kleber et al. (2015) [30]	56	2.58	0%*	67	46 (82%)	19 (34%)	37 (66%)	49 (88%)	46 (82%)
Vaquerizo et al. (2015) [48]	104	1.95	7%	65	78 (75%)	45 (43%)	34 (33%)	74 (71%)	68 (65%)
Cortese et al. (2015) [31]	156	2.83	3%	61	106 (68%)	55 (35%)	NR	91 (58%)	95 (61%)

Table 2 continued

Author	Number of patients	Mean vessel diameter (mm)	Bail out (%)	Mean age	Male *N* (%)	Diabetes *N* (%)	Smokers *N* (%)	HTN *N* (%)	Dyslip. *N* (%)
Ann et al., FFR and OCT (2016) [33]	20	2.68	0%*	59	13 (65%)	4 (20%)	7 (35%)	11 (55%)	9 (45%)
Ann et al., FFR and IVUS (2016) [32]	27	2.53	0%*	59	18 (64%)	7 (25%)	9 (32%)	15 (54%)	13 (46%)
Benezet et al. (2016) [41]	53	2.4	25%	66	35 (63%)	28 (50%)	24 (43%)	41 (73%)	30 (54%)
Uhlemann et al. (2016) [42]	76	NR (100% < 2.5)	4%	70	60 (79%)	33 (45%)	15 (20%)	73 (96%)	55 (72%)
Hee et al. (2017) [43]	65	NR	10%	66	56 (86%)	24 (37%)	30 (46%)	NR	NR
Poerner et al. (2017) [34]	46	2.32	6%	67	29 (63%)	18 (39%)	17 (37%)	40 (87%)	14 (30%)
Zivelonghi et al. (2017) [46]	35 de novo (143 total)	2.28	12%	67	120 (84%)	56 (39%)	29 (20%)	120 (84%)	118 (83%)
Cortese et al. DCB-RISE (2018) [50]	238 de novo (544 total)	2.84	12%	67	388 (71%)	177 (32%)	217 (40%)	413 (76%)	NR
Primary PCI (de novo lesions)									
Gobic et al. (2017) [51]	75 (DCB 38, DES 37)	2.6 (DCB), 3.04 (DES)	0%*	55	54 (72%)	6 (8%)	37 (49%)	19 (25%)	11 (14%)
Nijhoff et al. (2015) [52]	190 (DCB 40, BMS 51, DCB + BMS 50, DES 49)	2.83 (DCB), 2.84 (DCB + BMS), 2.84 (BMS), 2.78 (DES)	10%	58	150 (79%)	16 8%)	87 (46%)	64 (34%)	47 (25%)

Table 2 continued

Author	Number of patients	Mean vessel diameter (mm)	Bail out (%)	Mean age	Male *N* (%)	Diabetes *N* (%)	Smokers *N* (%)	HTN *N* (%)	Dyslip. *N* (%)
Ho et al. (2015) [53]	89	2.4	4%	59	74 (83%)	25 (28%)	50 [56]	49 (55%)	25 (28%)
Vos et al. (2014) [54]	100	3.02	41%	60	74 (74%)	11 (11%)	51 (51%)	29 (29%)	10 (10%)
Bifurcating lesions									
Kleber et al. (2016) [55]	64 (DCB 32, POBA 32)	DCB 2.38, POBA 2.41	9%	67	47 (73%)	23 (36%)	36 (56%)	NR	23 (36%)
Schulz et al. (2014) [56]	38	NR	13%	71	23 (61%)	17 (45%)	NR	35 (92%)	20 (53%)
Bruch et al. (2016) [57]	127	MB: 2.98, SB: 2.34	45%	66	102 (80%)	40 (32%)	43 (34%)	116 (91%)	96 (76%)
Vaquerizo et al. (2016) [58]	49	2.18	14%	62	38 (78%)	20 (41%)	22 (45%)	26 (53%)	30 (61%)
Her et al. (2016) [59]	16	MB: 2.72, SB: 1.25	0%	60	11 (68%)	4 (25%)	6 (38%)	7 (44%)	8 (50%)
Other clinical scenarios (calcifications and chronic total occlusions)									
Ito et al. (2017) [60]	81 (calcified 46, non-calcified 35)	2.22 calcified, 2.22 non-calcified	0%*	70	59 (73%)	49 (60%)	11 (14%)	60 (74%)	61 (75%)
Rissanen et al. (2017) [61]	65	NR	10%	72	44 (68%)	24 (37%)	25 (38%)	49 (75%)	58 (89%)
Köln et al. (2017) [62]	34	2.27	0%*	59	26 (73%)	8 (24%)	5 (15%)	25 (74%)	19 (56%)

DCB drug-coated balloon, *DES* drug-eluting stent, *POBA* plain-old balloon angioplasty, *BMS* bare metal stent, *HTN* hypertension, *Dyslip.* dyslipidemia, *N* number of patients, *NR* not reported, *MB* main branch, *SB* side branch

*Indicates studies were 0% bailout by design, i.e., they excluded patients receiving a bailout stent

discouraging results. Above all, the Dior I DCB has been shown to elute lower concentrations of paclitaxel compared to subsequent DCB generations. Also, adequate preparation of lesions with POBA before DCB application was only performed in 25% of lesions. Pre-dilatation with POBA and the use of cutting balloons has been shown to further facilitate intimal and medial drug delivery via the formation of microdissections [16]. Moreover, a high rate of bailout stenting was seen and may be attributed to use in type B dissections, which later recommendations do not advocate [14]. Furthermore '*geographical mismatch*' was not taken into account. This describes stented areas of the vasculature in bailout (with a BMS) that have not been previously treated with a DCB. They are particularly prone to restenosis and are associated with poorer outcomes. PEPCAD I previously also identified this [17, 18]. Geographical mismatch can be avoided through the use of a shorter stent implanted within the DCB treated area. A DES may be used in these cases or a BMS where long-term DAPT is contraindicated [14].

The BELLO study compared the IN.PACT Falcon DCB against the Taxus Liberté DES. It showed a smaller LLL in DCB-treated patients with comparable clinical outcomes to the DES [19, 20]. A sub-analysis of diabetic patients showed similar results [21]. However, issues arise when using LLL to compare stenting strategies with a balloon-only approach as stent placement, by nature, will result in greater acute luminal gain and consequently a greater LLL. Moreover, only a 1st-generation DES was the comparator. Giannini et al. showed comparable clinical outcomes in the BELLO DCB group when propensity score matched against patients treated with a 2nd-generation DES (Xience V or Promus) [22].

Nishiyama et al. [23] report comparable clinical outcomes between patients randomized to receive either SeQuent Please or a 2nd-generation DES (Xience Prime or Xpedition). This was largely due to a lack of adverse events seen in both groups over the short follow-up and the exclusion of DCB patients who received bailout stenting. The use of a Lacrosse non-slip element (NSE) balloon for pre-dilatation in addition to the use of intravascular ultrasound (IVUS) for the evaluation of an optimal result before DCB application, may have also contributed to the good outcomes. Shin et al. [24] compared SeQuent Please against a 2nd-generation DES (Xience Prime or Resolute Integrity). The investigators used a fractional flow reserve (FFR)-guided approach. Following POBA pre-dilatation, if a good FFR was seen (> 0.85) a DCB was used; otherwise a DES was implanted. Excellent clinical, angiographic, and functional results were seen. However, given the reservation of DES for more complex lesions, comparison is limited.

Sinaga et al. [25] retrospectively compared cohorts of SeQuent Please and 2nd/3rd-generation DES (Resolute Integrity, Xience, Promus Element, Biomatrix or Nobori)-treated patients. Comparable clinical outcomes were seen. However, the DCB-only treated group showed a significantly smaller MVD with DES use being associated with more proximal lesions of the major epicardial arteries. This could have confounded clinical outcomes with stenosis of smaller vessels perhaps having a less significant impact. Venetsanos et al. compared large propensity score-matched populations receiving a DCB (SeQuent Please, IN.PACT Falcon or Pantera Lux) against a 2nd/3rd-generation DES (Xience, Promus, Synergy, Resolute, Orsiro or Nobori). DCB treatment was notably associated with a significantly lower occurrence of TLT. This may be related to early discontinuation of DAPT as a minimum of only 6 months was required in the DES group [26]. DCB use was also seen in significantly less complex lesions, despite propensity score matching. A DES was used in the majority of bailout cases with good outcomes. DCB investigators were initially hesitant to do this due to concerns about the vascular effects of combining two drug-eluting devices. Her et al. showed a significantly lower incidence of periprocedural MI in propensity score-matched SeQuent Please treated patients when compared to 1st/2nd-generation DESs (Cypher, Taxus Express and Endeavor). However, 88.5% of DES patients were given only a first-generation device, which may explain the poorer outcomes seen. Periprocedural MI is a complication of up to 30% of DES procedures

and troponin release after PCI is classically associated with worse outcomes [27].

DCB vs. POBA

Funatsu et al. report a smaller LLL in SeQuent Please-treated patients when compared to POBA (with no significant difference in adverse outcomes) [28]. Sub-analysis showed significantly lower adverse clinical outcomes in patients predilated with a Lacrosse NSE. This may be related to significantly less bailout procedures being performed in this subgroup. A short follow-up period may also explain why POBA results were better than expected. Furthermore, bailout stenting was not indicated in residual stenosis up to 50% (as opposed 30%), with authors commenting that the German Consensus Group recommendations would have resulted in too aggressive a pre-dilatory approach, leading to a higher %bailout. The long-term effects of such an approach are unclear. Her et al. [29] also similarly report superior angiographic and comparable clinical outcomes when comparing SeQuent Please to POBA.

Moreover, in both studies, luminal enlargement was observed in over 50% of patients at follow-up. In a single-armed study, Kleber et al. [30] also found this in 69% of patients. This was most pronounced in areas where plaque burden was highest and was attributed to possible positive vessel remodelling, vascular healing and plaque regression. Cortese et al. [31] found that 94% of patients left dissection (type A–C) had later healed. To better characterize these positive remodeling processes, Ann et al. [32, 33] used IVUS histology and optical coherence tomography (OCT) in two cohorts of DCB-treated patients with a FFR-guided approach. Both studies showed good angiographic, functional, and clinical results. IVUS histological analysis showed the conversion of four thin-cap fibroatheromas to a thick-cap, suggesting possible plaque stabilization. OCT showed an increased mean luminal diameter and volume at follow-up in addition to the sealing of 66% of dissections. The OCTOPUS II study again through an FFR-guided approach with OCT analysis also showed positive luminal gain, healing of dissections and a lack of thin-cap fibroatheromas [34].

Registry Studies

Various registries exist to monitor the safety and efficacy of DCBs in the 'real world'. The majority of these have used SeQuent Please. The SeQuent Please worldwide registry is the largest of these and showed low MACE and TLR rates [35]. Bailout stenting was not associated with adverse outcomes however; diabetes was a significant predictor of TLR. The SeQuent Please Small Vessel PCB-only Registry reported slightly higher (but nonetheless good) MACE and TLR rates [36]. This was attributed to a smaller cohort MVD. Sub-analyses of this registry comparing elderly patients (> 75 years), patients with ACS and Asian versus Western populations have been published. Similar outcomes and %bailout was seen across all groups, despite the presence of more comorbidities in elderly patients and on average smaller vessels with longer lesions in Asian patients [37–39].

Other smaller SeQuent Please registries include Calé et al. [40], which showed a relatively high incidence of MACE and TLR despite a low frequency of bailout stenting. The authors attributed this to a high-risk population. Benezet et al., The Leipzig Registry, and Hee et al. all show favorable long-term MACE and TLR rates [41–43]. Cuculi et al. [44] report an IN.PACT Falcon DCB registry showing favorable %bailout, MACE, and TLR rates. Basavarajah et al's IN.PACT Falcon registry report a relatively high MACE and TLR rate. This was attributed to the presence of diffuse CAD (> 20 mm) in 80% of patients [45]. Zivelonghi et al. provide the longest follow-up seen in any DCB registry, showing good long-term MACE and TLR rates. Over half the cohort presented with ACS and this was associated with a higher incidence of adverse outcome [46].

Registries of the Dior II DCB include Valentines II. Here, angiographic follow-up was only performed in 34% of patients and showed a relatively high LLL (although low MACE and TLR rates were still seen) [47]. This may be due to recommended pre-dilatation being

performed in only 85% of patients. The Spanish Dior Registry similarly reported a high LLL. However, 54% of patients received the less effective Dior I balloon. Again, favorable clinical outcomes were reported and BMS bailout was a predictor of adverse events [48]. DELUX was a Pantera Lux DCB registry which showed comparable outcomes to other DCB registries, with BMS bailout again predicting poorer outcome [49]. The Italian Elutax SV Registry-DCB Rise is a registry of the Elutax SV DCB. It found low DOCE and TLR rates [50].

DCB-Only Angioplasty in PPCI

Study outcomes focusing on the use of DCB-only angioplasty for patients presenting with ACS are summarized in Table 4. In PPCI, the risk of ST occurrence with DES is greater than in elective cases due factors such as incomplete stent apposition and delayed tissue coverage, making the role of a DCB-only approach for this indication interesting to consider. Gobic et al. conducted a randomized trial, in ST elevation MI (STEMI) patients comparing SeQuent Please to the 3rd-generation DES Biomime. They showed a superior LLL in DCB-treated patients (although issues with LLL in stent versus balloon studies have been discussed) and comparable short-term clinical outcomes [51]. Luminal enlargement was also observed. However, DCB patients requiring BMS bailout were excluded from analysis. DCB patients also had a significantly smaller MVD compared to the DES group despite randomization. Nijhoff et al. [52] report an observational comparison of a DCB-only cohort against a previous three-armed randomized trial, DEB-AMI. DCB-only PCI exhibited a comparable LLL versus BMS and DCB + routine BMS, but was inferior to the Taxus Liberté DES. Despite this, comparable clinical outcomes were seen across all four groups. Coronary endothelial dysfunction (tested using acetylcholine) was also least pronounced in the DCB-only group. A lack of acute and late thrombosis indicates DCB-only may be viable in STEMI patients with a long-term DAPT contraindication. PAPPA was a feasibility study of the DCB-only approach (using Pantera Lux) in STEMI showing favorable TLR and MACE rates. However, a very high bailout rate of 41% was seen, due to a high rate of dissections, which may be related to the use of a slightly oversized balloon for pre-dilatation [53]. Ho et al. [54] report acceptable short-term clinical outcomes in STEMI patients treated with SeQuent Please. It should be noted that DCB-only PPCI investigators have commented on the importance of thrombus aspiration where relevant before DCB application to avoid reduced paclitaxel transfer by an interposed mural thrombus.

DCB-Only Angioplasty in Bifurcation

Table 5 provides a summary of the DCB-only studies which focus on bifurcating lesions. Bifurcation represents around 20% of PCI procedures and is associated with a higher risk of restenosis and complications. Both the interventional approach and operator factors are highly important for a successful procedure. DCB-only PCI in bifurcation theoretically provides certain advantages over stenting strategies. These include the maintenance of a natural flow distribution and avoidance of plaque and carina shift due to the absence of a stent overstretching and straightening the distal vessel, which predisposes to side-branch occlusion or narrowing, leading to adverse clinical events. PEPCAD-BIF compared SeQuent Please against POBA in a randomized study. The DCB group showed a significantly smaller LLL, however comparable clinical outcomes were nonetheless seen [55]. Bifurcating lesions involving the proximal main-branch (Medina class 1,X,X) were, however, notably excluded. Various single-armed studies have also been conducted reporting acceptable MACE and TLR rates [56, 57]. Bruch et al. report a cohort where 75% of patients presented with true bifurcation (Medina 1,1,1, 1,0,1, or 0,1,1). Although not associated with worse clinical outcomes, a high %bailout of 45% was seen and this was associated with lesions of the left anterior descending (LAD) artery and the presence of B2/C lesions. Vaquerizo et al. report clinical and angiographic outcomes in ostial side-branch (SB) lesions

Table 3 DCB-only angioplasty in general de novo coronary lesions

Author	DCB used (comparator)	Angiographic outcome (FU, %FU)	Clinical outcome (FU, %FU)	Duration of DAPT
Randomized studies				
Cortese et al. PICCOLETO Study (2010) [15]	Dior I (1st-Gen DES)	%DS: DCB 43.6% vs. DES 24.3%, $p = 0.029$ (6 months, 95%)	MACE: DCB 35.7% vs. DES 13.8%, $p = 0.054$; TLR: DCB 32.1% vs. DES 10.3%, $p = 0.15$ (9 months, 95%)	DCB 1 month, Bailout BMS 3 months, DES 12 months
Latib et al. BELLO Study (2012, 2015) [19, 20]	IN.PACT Falcon (1st-Gen DES)	In-stent/balloon LLL: DCB 0.08 ± 0.38 vs. DES 0.29 ± 0.44 $p < 0.001$ (6 months, 89.6%)	MACE*: DCB 14.8% vs. DES 25.3%, $p = 0.08$ TLR: DCB 6.8% vs. DES 12.1%, $p = 0.23$ (24 months, 98.4%)	DCB 1 months, bailout BMS 3 months, DES 12 months
Nishiyama et al. (2016) [23]	SeQuent Please (2nd-Gen DES)	LLL: DCB 0.25 ± 0.25 vs. DES 0.37 ± 0.40 $p = 0.185$ (8 months, 100%)	MACE: DCB 0% vs. DES 6.1% TLR: DCB 0% vs. DES 6.1%, $p = 0.193$ (8 months, 100%)	DCB and DES 8 months
Funatsu et al. (2017) [28]	SeQuent Please (POBA)	In-balloon LLL: DCB 0.01 ± 0.31 vs. POBA 0.32 ± 0.34), $p < 0.01$ (6 months, 95%)	TVF: DCB 3.4% vs. POBA 10.3%, $p = 0.2$ TLR: DCB 2.3% vs. POBA 10.3%, $p = 0.07$ (6 months, 95%)	3 months
Comparative observational studies				
Her et al. (2016) [29]	SeQuent Please (POBA)	LLL: DCB − 0.12 ± 0.30 vs. POBA 0.25 ± 0.50 $p < 0.001$ (9 months, 100%)	TLR: DCB 0% vs. POBA 4.3%, $p = 0.229$ (9 months, 100%)	1.5 months
Shin et al. (2016) [24]	SeQuent Please (2nd Gen DES/BMS)	LLL: DCB 0.05 ± 0.27 vs. DES/BMS 0.40 ± 0.54 $p = 0.022$ (9 months, 79%)	MACE: DCB 0% vs. DES/BMS 9%, p N.S. TLR: DCB 0% vs. DES/BMS 5%, p N.S. (12 months, 100%)	DCB 1.5 months, bailout BMS 6 months, DES 12 months
Sinaga et al. (2016) [25]	SeQuent Please (2nd/3rd-Gen DES)	NR	MACE: DCB 11.6% vs. DES 11.7%, $p = 1.000$ TLR: DCB 5.2% vs. DES 3.7%, $p = 0.601$ (12 months, 100%)	DCB 6 months, DES 12 months

Table 3 continued

Author	DCB used (comparator)	Angiographic outcome (FU, %FU)	Clinical outcome (FU, %FU)	Duration of DAPT
Giannini et al. (2017) [22]	IN.PACT Falcon (2nd-Gen DES)	NR	MACE*: DCB 12.2% vs. DES 15.4%, $p = 0.538$ TLR: DCB 5.6% vs. DES 4.4%, $p = 0.720$ (12 months, 100%)	DCB 1 month, Bailout BMS 3 months, DES 12 months
Her et al. (2017) [27]	SeQuent Please (1st/2nd Gen DES)	NR	Pericprocedural MI: DCB 1.9% vs. DES 23.1% $p = 0.002$ TLR: DCB 1% vs. DES 0%, $p = 1.00$ (12 months, 100%)	DCB 1.5 months, DES 12 months
Venetsanos et al. (2018) [26]	SeQuent Please, Pantera Lux, IN.PACT Falcon (2nd/3rd-Gen DES)	NR	TLR: DCB 0.2% vs. DES 1.1%, HR: 1.05; (95% CI 0.72–1.53) TLT: DCB 7.0% vs. DES 6.2%, HR: 0.18 (95% CI 0.04–0.82) (30 months, 100%)	DCB 1 month, DES 6 months
Single-armed observational studies				
Unverdorben et al. PEPCAD I (2010, 2013) [17, 18]	SeQuent Please	In-Segment LLL: 0.28 ± 0.53 (6 months, 89%)	MACE: 15.3% TLR: 11.9% (36 months, 100%)	DCB 1 month, bailout BMS 3 months
Cuculi et al. (2012) [44]	IN.PACT Falcon	NR	TLR: 4.8% (12 months, 95%)	1.5 months
Woehrle et al. SeQuent Please World Wide Registry (2012) [35]	SeQuent Please	NR	MACE: 2.6% TLR: 1.0% (9 months, 100%)	1 month
Calé et al. (2013) [40]	SeQuent Please	NR	MACE: 14.7% TLR: 4.0% (12 months, 100%)	3 months
Waksman et al. Valentines II (2013) [47]	Dior II	In-Balloon LLL: 0.38 ± 0.39 (7.5 months, 34%)	MACE: 8.7% TLR: 2.9% (6–9 months, 100%)	DCB 3 months, bailout BMS NR

Table 3 continued

Author	DCB used (comparator)	Angiographic outcome (FU, %FU)	Clinical outcome (FU, %FU)	Duration of DAPT
Basavarajah et al. (2014) [45]	IN.PACT Falcon	NR	MACE*: 16.5% TLR: 17.7% (15 months, 100%)	DCB 1 month, Bailout BMS 3 months, DES 12 months
Toelg et al. DELUX Registry (2014) [49]	Pantera Lux	NR	MACE*: 9.4% TLR: 3.1% (12 months, 91%)	DCB 3 months
Zeymer et al. SeQuent Please Small Vessel 'PCB Only' Registry (2014) [36]	SeQuent Please	NR	MACE: 4.7% TLR: 3.6% (9 months, 100%)	1 month
Kleber et al. (2015) [30]	SeQuent Please, IN.PACT Falcon	In-balloon MLD: PP 1.73 ± 0.55 vs. FU 1.86 ± 0.5, $p = 0.012$ (4 months, 100%)	MACE: 1.8% TLR: 0% (4 months, 100%)	1 month
Vaquerizo et al., Spanish Dior Registry (2015) [48]	Dior I/II	In-stent/balloon LLL: 0.31 ± 0.2 (6–8 months, 84%)	MACE: 6.7% TLR: 2.9% (12 months, 100%)	DCB 1 month, bailout BMS NR
Cortese et al. (2015) [31]	Restore Elutax SV	Dissection cohort LLL: 0.14 ± 0.28 (6 months, 100%)	MACE: 7.2. % TLR: 5.3% (9 months, 100%)	DCB 1 month, bailout stent 6 months
Ann et al. FFR and OCT (2016) [33]	SeQuent Please	In-balloon LLL: 0.01 ± 0.21 (9 months, 100%)	MACE: 0% TLR: 0% (9 months, 100%)	NR
Ann et al. FFR and IVUS (2016) [32]	SeQuent Please	In-balloon LLL: 0.02 ± 0.27 (9 months, 100%)	MACE: 0% TLR: 0% (9 months, 100%)	1.5 months
Benezet et al. (2016) [41]	SeQuent Please	NR	MACE*: 8.9% TLR: 5.4% (36 months, 100%)	DCB 1 months, bailout BMS 6 months
Uhlemann et al. Leipzig Registry (2016) [42]	SeQuent Please	NR	MACE*: 13% TLR: 0% (27 months, 100%)	3 months

Table 3 continued

Author	DCB used (comparator)	Angiographic outcome (FU, %FU)	Clinical outcome (FU, %FU)	Duration of DAPT
Hee et al. (2017) (2017) [43]	SeQuent Please	NR	MACE*: 1% TLR: 0% (16 months, 100%)	DCB 3 months, bailout BMS 6 months, bailout DES 12 months
Poerner et al. OCTOPUS II (2017) [34]	SeQuent Please	LLL: − 0.13 ± 0.44 (6 months, 85%)	MACE: 6.5% TLR: 4.3% (12 months, 100%)	DCB 1 month
Zivelonghi et al. (2017) [46]	IN.PACT Falcon	NR	MACE*: 14.3% TLR: 11.4% (48 months, 100%)	DCB 1 month, bailout DES 6 months
Cortese et al. Italian Elutax SV rEgistry-DCB-RISE (2018) [50]	Elutax SV	NR	DOCE: 2.6% TLR: 2.6% (13 months, 93.2)	3 months

DCB drug-coated balloon, *DES* drug-eluting stent, *POBA* plain-old balloon angioplasty, *BMS* bare metal stent, *Gen* generation, *FU* follow-up, *%FU* percentage follow-up, *DAPT* dual anti-platelet therapy, *%DS* percentage diameter stenosis, *LLL* late luminal loss, *TLR* target lesion revascularization, *MACE* major adverse cardiovascular events, *MI* myocardial infarction, *TLT* target lesion thrombosis, *MLD* minimum luminal diameter, *DOCE* device-orientated adverse cardiovascular events, *TVR* target vessel revascularization, *PP* post procedure, *HR* hazard ratio, *NS* non-significant, *NR* not reported
*Indicates studies that adopted a different definition for the composite outcome of MACE and these are elaborated upon in Appendix B

(Medina 0,0,1) treated with Dior II and found high MACE and TLR rates [58]. PCI of ostial side-branch lesions is naturally associated with a smaller vessel diameter, greater incidence of recoil, lower acute luminal gain and thus a higher rate of complications. Her et al. found late luminal gain (confirmed on OCT analysis) in both the main-branch (MB) and SB of bifurcating lesions treated with SeQuent Please [59]. No adverse events were reported. Lesions that showed poor image quality due to dissection or artifact on OCT were notably excluded.

DCB-Only Angioplasty in Other Clinical Scenarios

Table 6 outlines the studies focusing on DCB-only angioplasty in other clinical scenarios, namely in calcification and CTO. Heavily calcified CAD is associated with poorer clinical outcomes due to the difficulty of adequately deploying a stent due to incomplete stent expansion and strut apposition. Calcification is especially problematic in patients with chronic kidney disease. Ito et al. [60] show acceptable MACE and TLR rates in a feasibility study. Preparation of the calcified lesion required rotational atherectomy in 80% of patients. Chronic hemodialysis (seen in 21% of patients) was associated with an increased risk of adverse events. Comparable clinical and angiographic results were seen when compared to patients with non-calcified lesions. These favorable results may be explained by the exclusion of patients with significant residual stenosis and dissection following lesion preparation as well as the use of IVUS and OCT to aid the procedure

Table 4 DCB-only angioplasty in primary PCI for de novo lesions

Author	Design	DCB used	Angiographic outcome (FU, %FU)	Clinical outcome (FU, %FU)
Gobic et al. (2017) [51]	Randomized trial, DCB vs. 3rd-Gen DES	SeQuent Please	LLL: DCB − 0.09 ± 0.09 vs. DES 0.1 ± 0.19, $p < 0.05$ (6 months, 84%)	MACE*: DCB 5.3% vs. DES 5.4%, p NS TLR: 0% DCB vs. 5.4% DES, p NS (6 months, 100%)
Nijhoff et al. DEB-AMI (2015) [52]	Comparative observational study, DCB only vs. DCB + BMS vs. BMS vs. 1st-Gen DES	Dior II	In Balloon/Stent LLL: DCB 0.51 ± 0.59 vs. DCB + BMS 0.64 ± 0.56 $p = 0.33$ vs. BMS 0.74 ± 0.32 $p = 0.08$ vs. DES 0.2 1 ± 0.32 $p < 0.01$ (6 months, 90%)	MACE*: DCB 17.5% vs. DCB + BMS 23.9% vs. BMS 25.0% vs. DES 4.4% p NS TLR: DCB 12.5% vs. DCB + BMS 23.9% vs. BMS 19.1% vs. DES 2.2%, p NS (12 months, 100%)
Vos et al. PAPPA (2014) [53]	Single-armed observational study	Pantera Lux	NR	MACE*: 5% TLR: 3% (12 months, 100%)
Ho et al. (2015) [54]	Single-armed observational study	SeQuent Please	NR	MACE: 4.5% TVR: 0% 1 month (100%)

DCB drug-coated balloon, *DES* drug-eluting stent, *BMS* bare metal stent, *Gen* generation, *FU* follow-up, *%FU* percentage follow-up, *LLL* late luminal loss, *TLR* target lesion revascularization, *MACE* major adverse cardiovascular events, *TVR* target vessel revascularization, *NS* non-significant, *NR* not reported

*Indicates studies that adopted a different definition for the composite outcome of MACE and these are elaborated upon in Appendix B

and the use of a Lacrosse NSE for pre-dilatation. Rissanen et al. [61] report outcomes in 65 patients with calcified lesions treated with SeQuent Please, following rotational atherectomy. It is thought that rotational atherectomy prior to DCB treatment reduces calcific burden, thus enhancing the penetration of paclitaxel into the vessel wall. This technique has already been established in calcified femoro-popliteal lesions. CTOs are defined as a coronary occlusion without anterograde flow that has been present for at least 3 months. It has a reported incidence of up to 30% and is associated with higher rates of ISR and ST in addition to being technically challenging for interventionalists. In Köln et al.'s [62] feasibility study, favorable angiographic results were seen. A lack of MI, vessel thrombosis, or death at follow-up are also significant findings. However, this study excluded patients who did not achieve satisfactory pre-dilatation and only included patients requiring an anterograde interventional approach.

DISCUSSION

This was a systematic review of 41 studies employing a DCB-only approach for the treatment of de novo CAD. These consisted of randomized trials and comparative observational studies that compared DCB-only against DES or POBA, in addition to single-armed observational studies (mostly registries). The majority

Table 5 DCB-only angioplasty in de novo coronary bifurcating lesions

Author	Design	DCB used	Angiographic outcome (FU, %FU)	Clinical outcome (FU, %FU)	Duration of DAPT
Kleber et al. PEPCAD-BIF (2016) [55]	Randomized trial, DCB vs. POBA	SeQuent Please	In-Segment LLL: DCB 0.08 ± 0.31 vs. POBA 0.47 ± 0.61 p = 0.006 (9 months, 75%)	MACE: DCB 3.1% vs. POBA 12.5%, p N.S TLR: DCB 3.1% vs. POBA 9.4%, p N.S (9 months, 100%)	1 month, bailout BMS/DES 12 months
Schulz et al. (2014) [56]	Single-armed observational study	SeQuent Please, IN.PACT Falcon	Binary restenosis: 10% (4 months, 77%)	MACE: 7.7% TLR: 7.7% (4 months, 100%)	1 month
Bruch et al. (2016) [57]	Single-armed observational study	SeQuent Please	NR	MACE*: 6.1% TLR: 4.5% (9 months, 100%)	1 month, bailout BMS 6 months
Vaquerizo et al. (2016) [58]	Single-armed observational study	Dior II	In-balloon LLL: 0.32 ± 0.7 (7–8 months, 63%)	MACE*: 16.3%, TLR: 14.3% (12 months, 82%)	1 month
Her et al. (2016) [59]	Single-armed observational study	SeQuent Please	MB LLL: − 0.01 ± 0.18, SB LLL: − 0.02 ± 0.22 (9 months, 100%)	MACE: 0% (9 months, 100%)	1.5 months

DCB drug-coated balloon, *DES* drug-eluting stent, *POBA* plain-old balloon angioplasty, *BMS* bare metal stent, *Gen* generation, *FU* follow-up, *%FU* percentage follow-up, *DAPT* dual anti-platelet therapy, *LLL* late luminal loss, *TLR* target lesion revascularization, *MACE* major adverse cardiovascular events, *MB* main branch, *SB* side branch, *NS* non-significant, *NR* not reported

*Indicates studies that adopted a different definition for the composite outcome of MACE and these are elaborated upon in Appendix B

of studies investigate DCB-only angioplasty in all patients with de novo CAD, however some studies focus on specific interventional scenarios. The vast majority of all DCB-only studies have been conducted in small vessels (< 2.8 mm) as DES therapy for this indication is currently suboptimal.

DCB-Only Angioplasty in General De Novo CAD

Comparison of the DCB-only approach against the DES is essential to consider, given the DES forms the current mainstay in de novo CAD treatment. With the exception of the PICCOLETO study, DCB-only and DES PCI show similar clinical outcomes [15]. Despite these encouraging results, the literature is largely lacking in data from randomized trials that compare to a 2nd- or 3rd-generation DES, with Nishiyama et al. [22] providing the only such general de novo CAD study. Longer-term data is also needed. The finding of a reduced risk of thrombosis and peri-procedural MI in comparative observational studies is also of interest [26, 27]. Although reasons for why these results were seen have been speculated, further investigation in a randomized setting would be of use.

Table 6 DCB-only angioplasty in other clinical scenarios

Author	Design	DCB used	Angiographic outcome (FU, %FU)	Clinical outcome (FU, %FU)	Duration of DAPT
Calcified lesions					
Ito et al. (2017) [60]	Comparative observational calcified vs. non-calcified lesions	SeQuent Please	LLL: Calcified 0.03 vs. non-calcified − 0.18, $p = 0.093$ (6 months, 73%)	MACE: 18.6% calcified vs. 11.5% non-calcified, $p = 0.57$ TLR 14.7% vs. 6.6%, $p = 0.64$ (24 months 100%)	3 months
Rissanen et al. (2017) [61]	Single-armed observational study	SeQuent Please	NR	MACE*: 20% TLR: 3.1% (24 months, 100%)	1 month
Chronic total occlusions					
Köln et al. (2017) [62]	Single-armed observational study	SeQuent Please, IN.PACT Falcon	MLD: PP 1.69 ± 0.31 vs. FU 1.59 ± 0.57 $p = 0.954$ (8 months, 100%)	MACE: 17.6%, TLR: 17.6% (8 months, 100%)	1 month

DCB drug-coated balloon, *DES* drug-eluting stent, *BMS* bare metal stent, *FU* follow-up, *%FU* percentage follow-up, *DAPT* dual anti-platelet therapy, *LLL* late luminal loss, *TLR* target lesion revascularization, *MACE* major adverse cardiovascular events, *MLD* minimal luminal diameter, *PP* post procedure, *NR* not reported

*Indicates studies that adopted a different definition for the composite outcome of MACE and these are elaborated upon in Appendix B

Furthermore, deriving conclusions on the angiographic superiority of a DCB-only approach versus the DES is difficult, as the majority of studies used LLL, which naturally favors DCB-only PCI. LLL as an angiographic endpoint should no longer be used due to the larger acute luminal gain seen in DESs, rather studies can use %DS (which is less influenced by this) or focus on clinical MACE and TLR as primary endpoints. This being said, given the low rate of adverse clinical outcomes occurring in all PCI procedures, comparison between a DCB-only approach and DES may be difficult to characterize based on these alone. As such, angiographic data still have an important role to play. Additionally, the emergence of studies using intravascular imaging such as OCT and IVUS has been useful in further characterizing the benefits of a DCB-only approach on the vasculature. Moreover, their use to guide the DCB-only procedure and to ensure a satisfactory result has been associated with improved outcomes [32–34]. Future research should continue to adopt these techniques to supplement angiographic data where possible.

Studies comparing the use of DCB-only PCI versus POBA have shown superior angiographic outcomes as expected, however MACE and TLR rates were largely similar and this may be attributed to a short follow-up period in these studies. Although studies comparing POBA are useful to characterize the additional benefits of drug elution, their scope for influencing clinical practice is limited. As such, there should be less emphasis placed on the importance of further such investigation.

There is a wealth of registry data regarding the use of a DCB-only approach for the

treatment of de novo CAD. However, their rates of clinical events are highly heterogeneous. This may be attributed to a large variation in follow-up period, patient characteristics, rates of bail-out stenting and experiential and operator factors. A lack of true consensus for the definition of the composite clinical outcome MACE may also be of importance.

DCB-Only Angioplasty in Specific Clinical Scenarios

Data regarding the use of a DCB-only approach in PPCI are promising, with Gobic et al. [51] showing comparable short-term clinical outcomes to a 3rd-generation DES in a randomized study. Additional longer-term studies are required to further characterize this. Conversely, the use of a DCB-only approach in bifurcation is limited by a lack of data in lesions involving the proximal MB in addition to a lack of randomised studies comparing to DES therapy of any kind. The current strategic mainstay of bifurcation PCI is through MB stenting with provisional stenting of the SB. Ideally, randomized studies specifically comparing these two strategies are needed. The use of DCB-only PCI in the treatment of calcified lesions and CTOs is still in its infancy, with only a small number of single-armed studies that at best point towards possible feasibility as opposed to efficacy.

Duration of DAPT

As expected, due to a lack of foreign body placement in the vasculature, a DCB-only approach was associated with a shorter duration of DAPT of 1–3 months when compared to DESs, which typically required a minimum of 12 months. Given that the majority of studies show comparable clinical outcomes between DCB-only and DES PCI, the shorter duration of DAPT appears to be well tolerated. This presents a key advantage of a DCB-only strategy, especially in cases where long-term DAPT is contraindicated. It should be noted that for the treatment of ACS, DAPT is given for 12 months according to European guidelines, thus the benefit of reducing DAPT for the purposes of PPCI has not been seen [4].

FUTURE PERSPECTIVES

Although current data are promising, there is still a need for further long-term randomized control trial data comparing a DCB-only approach against a 2nd/3rd-generation DES. An example of such a study, BASKET-SMALL 2, has recently been published. It compared SeQuent Please to the 2nd-generation DESs Xience and Taxus Element in 758 patients. Comparable, low MACE rates at 12 months of 7.5% (DCB) vs. 7.3% (DES) were seen, showing non-inferiority of the DCB-only approach [63]. Future, emerging areas of interest include the use of FFR to guide intervention in DCB-only angioplasty and the use of the Lacrosse NSE for pre-dilatation, which have both shown good results. The randomized REVELATION study will compare 120 STEMI patients treated with DCB-only angioplasty versus DES using FFR with a primary endpoint of MACE at 5 years [64]. Its findings are awaited with great interest. Furthermore, DCBs using drugs other than paclitaxel are also beginning to be seen, with the MagicTouch Sirolimus-coated balloon recently gaining approval. These may prove to be superior to the current paclitaxel DCBs and characterization of this will be of great significance.

CONCLUSIONS

The treatment of de novo CAD using a DCB-only approach has shown promising data in SVD, with comparable clinical outcomes to DESs specifically in general de novo CAD and STEMI. Drug elution to a vascular lesion in the absence of a foreign-body placement, such as a stent, poses certain advantages over the DES such as positive remodeling and of even greater clinical relevance; a shorter duration of DAPT therapy, favoring use in those with a contraindication to long-term DAPT. Areas where further research should proceed have been identified and there is a specific need for longer-

term randomized trials that compare DCB-only PCI against a 2nd/3rd-generation DES. DCB-only angioplasty is also beginning to see use in other challenging interventional scenarios such as bifurcation, CTOs, and calcified lesions, although further evidence for these specific indications is needed.

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