Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2023i1.468
*Biol. Clin. Sci. Res. J., Volume, **2023**: 468*
Original Research Article

DRUG-COATED BALLOONS FOR THE TREATMENT OF STENT EDGE RESTENOSIS

JAN MW[1], IKRAMULLAH S[*2], MAGSI M[3], HADEE A[4], KHAN N[5], SAFDAR T[6]

[1]*Department of Cardiology, Peshawar Institute of Cardiology Hayatabad Peshawar, KPK, Pakistan*
[2]*Cat-C Hospital Wari Dir Upper, KPK, Pakistan*
[3]*Department of Cardiology, Shaikh Muhammad Bin Zayant al Nahyan Institute of Cardiology Quetta, Balochistan, Pakistan*
[4]*Department of Cardiology, CMH Muzaffarabad, AJK, Pakistan*
[5]*Demonstrator Pharmacology, PGMI/AMC, Lahore, Punjab, Pakistan*
[6]*Department of Medicine, Fauji Foundation Hospital Rawalpindi, Punjab, Pakistan*
**Correspondence author email address:* dr.Ikram96@gmail.com

(Received, 25th June 2023, Revised 19th September 2023, Published 16th October 2023)

Abstract: *This study aimed to compare the effectiveness of Drug-Coated Balloon (DCB) treatment with New-Generation Drug-Eluting Stent (DES) implantation for Stent Edge Restenosis (SER). The study was conducted at LRH Peshawar from 11-02-2022 to 11-02-2023 and included 130 patients with stent edge restenosis. Ethical approval was obtained from the hospital's ethical committee, and informed consent was taken from all patients. Patients were divided into two groups, Group A (DES) and Group B (DCB), and their clinical outcomes were analyzed using propensity score matching (PSM). The study showed that DCB therapy reduced the risk of target lesion revascularization (TLR) compared to DES during a median follow-up period of 1080 days. After conducting PSM, there was no significant difference in the risk of TLR between the two groups. Moreover, there were no significant differences in the risk of all-cause death, major adverse cardiovascular events (MACE), or TLR between Group A and Group B. In conclusion, DCB treatment for SER was found to be equally as effective as new-generation DES following PSM. Therefore, DCB can be considered a viable alternative to the new-generation DES for treating SER.*

Keywords: Drug-Coated Balloon, Drug-Eluting Stents, Coronary Restenosis, Stent Edge Restenosis

Introduction

Drug-coated balloons (DCBs) are medical devices that treat various vascular conditions, including stent edge restenosis (Lin et al., 2018; Zhang and Chen, 2020). Stent edge restenosis refers to re-narrowing a blood vessel at the edges of a previously implanted stent (Ullrich et al., 2021). This condition is attributed to the increase in smooth muscle cell growth and the accumulation of scar tissue (known as neointimal hyperplasia) at the stent's edges. ISR is affected by a range of factors, including biological, genetic, mechanical, and technical elements.(Jensen et al., 2018)

The latest generation of drug-eluting stents (DES) has demonstrated advancements compared to the initial generation of DES, particularly in decreasing the likelihood of in-stent restenosis (ISR) and thrombosis (Byrne et al., 2015).

Furthermore, performing a repeat revascularization procedure for ISR carries a substantial risk of recurrent ischemic events. (Tamez et al., 2021) Stent edge restenosis (SER) represents a form of ISR that occurs specifically at the stent's edge, making it the primary challenge associated with ISR after stent placement. Studies have suggested that the development of SER is linked to factors such as vessel trauma from balloon inflation or stent deployment, the presence of remaining plaque, and the reduced luminal space in the stent's edge regions (Ino et al., 2016; Kim et al., 2013; Kitahara et al., 2017). Moreover, mechanical stresses resulting from hinge movement have been identified as contributing to the risk of SER occurrences (Jimba et al., 2021).

Drug-coated balloons (DCB) are medical devices used in interventional cardiology and designed to treat narrowed or blocked blood vessels, particularly arteries. Drug-coated balloons (DCB) administer lipophilic anti-proliferative drugs directly into the target vessel to inhibit neointimal hyperplasia without including a metal stent or polymer. It is widely acknowledged that utilizing DCBs offers a beneficial strategy for treating de-novo coronary small vessel disease (Cortese et al., 2020; Jeger et al., 2020b; Song et al., 2020). Numerous studies have illustrated the efficacy and safety of drug-coated balloons (DCBs) in addressing in-stent restenosis (ISR) (Giacoppo et al., 2020; Kokkinidis et al., 2018). Nevertheless, there remains uncertainty about the results of using DCBs for SER. So, this research study examines the clinical consequences following the application of DCBs in SER cases compared to the latest-generation DES. The study aimed to compare the clinical outcomes of Drug-Coated Balloon (DCB) use for treating Stent Edge Restenosis (SER) with New-Generation Drug-Eluting Stent (DES) implantation.

Methodology

The following cross-sectional study was conducted at LRH, Peshawar, over one year from February 2022 to February 2023. The study focused on patients with stent edge restenosis aged between 40 and 80 years, regardless of gender. To ensure the quality of the study, certain selection criteria were put in place. Patients who had only received medical therapy or coronary bypass surgery (CABG) were

excluded, as were patients with medical conditions that made using antithrombotic drugs inadvisable. Also excluded were patients who underwent PCI with both DCB and DES in a single coronary artery and those who had angioplasty in a saphenous vein graft during PCI.

Approval for the ethical aspects of this study was obtained from the hospital's ethics committee. After approval, this study was conducted in the cardiology department of Lady Reading Hospital Peshawar. All patients who met the inclusion criteria and presented to the cardiology department were included in the study, and informed consent was obtained from all enrolled participants. The pros and cons of the present study were explained in their native language before signing the informed consent. The enrolled patients were physically examined. The patients were categorized into two groups: Group A, which received treatment with SeQuent Please DCB, and Group B, which received DES treatment. Group A patients were treated with SeQuent Please DCB coated with paclitaxel, while Group B patients were treated with the following new-generation stents: Xience, Ultimaster, Synergy, Resolute, and Orsiro. The data of all the registered patients was gathered from hospital records, clinical appointments, and telephone consultations. PCI was carried out using best clinical practice guidelines. All patients received 100U/kg of intravenously given unfractionated heparin before PCI.

Throughout the process, the active clotting time was kept at or above 300 seconds. DCB was used in accordance with the noted recommendations. We performed the DCB angioplasty as recommended, utilizing an inflation duration of at least 60 seconds and an inflation pressure of at least 6. Throughout the PCI procedures, all patients underwent imaging procedures, including intravascular ultrasonography and optical coherence tomography (OCT). The operators choose the device size, balloon pressure, and inflation time, as well as the lesion preparation, pre-dilatation balloon choice (using a semi-compliant balloon, non-compliant balloon, or scoring balloon before DCB or DES), and scoring balloon or non-scoring balloon pre-dilatation balloon selection. Throughout the procedures, the operators had the discretion to determine whether to utilize the imaging device and perform post-dilatation. Following PCI, group A and B patients were treated with dual antiplatelet therapy (DAPT) for at least 6 months.

Data entry and analysis were conducted using Statistical Package for Social Sciences (SPSS) version 23. The data was then displayed in tabular format, presenting Mean ± SD for continuous variables and frequency and percentage for categorical variables.

Results

There were 130 patients with a mean age of 43.67+9.47 years in the DCB group and 44.3+10.19 years in the DES group, with an insignificant P-value of 0.68. In group A, there were 32 (46.3%) and 34 (54.0%) male and female, respectively, and in group B, there were 36 (53.7%) and 29 (46.0%) male and female, respectively, with P-value of 0.38. The baseline characteristics of all the patients before propensity matching are shown in Table 1, while the Angiographic characteristics of all the patients before propensity matching are shown in Table 2. All patients' Procedural characteristics before propensity matching both groups with P-value is shown in table 3-0.

Several key variables were examined in this comparative analysis of patients undergoing different vascular interventions, including Drug-Coated Balloon (DCB) and Drug-Eluting Stent (DES) procedures. While no statistically significant differences were observed in dilatation, non-compliant balloons, intravascular ultrasound, optical coherence tomography (OCT), post-diameter stenosis, and follow-up angiography between the DCB and DES groups, significant distinctions emerged. Notably, patients in the DCB group had a smaller mean diameter but a longer mean length for their vascular devices than the DES group. Additionally, DES procedures employed a higher maximal pressure on average. Furthermore, the follow-up duration was significantly longer for the DCB group than for the DES group. These findings provide valuable insights into the procedural variances and outcomes associated with DCB and DES interventions, which can inform clinical decision-making and patient care strategies in the context of vascular treatments (table 3).

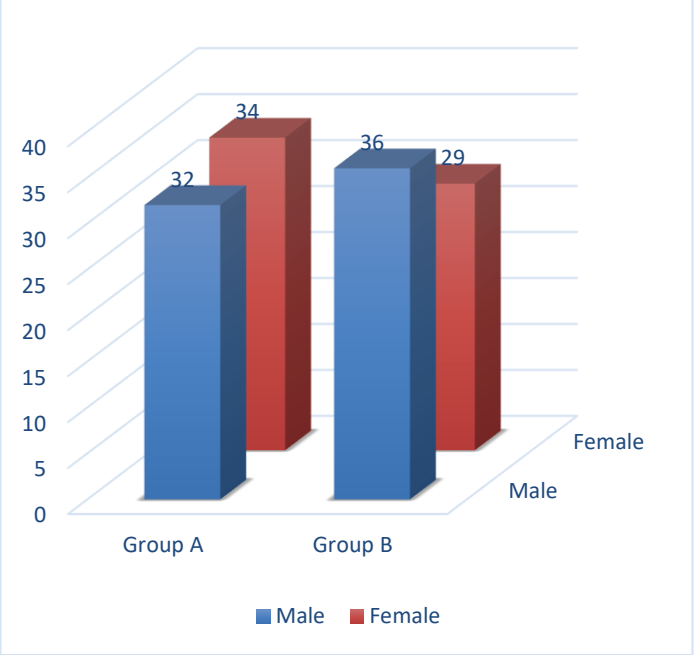

Fig 1: Bar chart showing gender-wise distribution in both groups.

Table 1: Baseline characteristics of all the patients before propensity matching (n=130)

Variables	DCB (n = 65)	DES (n = 65)	P-Value
Age (years)	43.67(9.47)	44.3(10.19)	0.68
Gender			
Male	32 (46.3%)	36 (53.7%)	0.38
Female	34 (54.0%)	29 (46.0%)	

[Citation: Jan, M.W., Ikramullah, S., Magsi, M., Hadee, A., Khan, N., Safdar, T. (2023). Drug-coated balloons for the treatment of stent edge restenosis. *Biol. Clin. Sci. Res. J.*, **2023***: 468*. doi: https://doi.org/10.54112/bcsrj.v2023i1.468]

BMI	22.72 (3.85)	23.0 (3.761)	0.41
LVEF	54.64 (6.63)	52.84 (6.53)	0.12
Hypertension	53(81.5%)	55 (84.6)	0.03
Diabetes	34(52.3%)	50 (76.9%)	0.00
Dyslipidemia	41 (63.1%)	44 (67.7%)	0.48
Family history	29 (44.6%)	30 (46.2%)	0.86
Smoking	26 (40.0%)	28 (43.1%)	0.72
ACS	11 (16.9%)	16 (24.6%)	0.28
CKD	10 (15.4%)	13 (20.0%)	0.57
Hemodialysis	4 (6.2%)	8 (12.3%)	0.22
PVD	15 (23.1%)	19(29.2%)	0.45
Prior CABG	8 (12.3%)	5 (7.7%)	0.38
Prior MI	19 (29.2%)	12(18.5%)	0.15
Atrial fibrillation	9 (13.8%)	11 (16.9%)	0.62
LVEF	54.64 (6.63)	52.84 (6.53)	0.12
Prior DES	55 (84.6%)	52 (80.0%)	0.49
Prior BMS	19 (29.2%)	13 (20.0%)	0.22
Medications			
Aspirin	54 (83.1%)	53 (81.5%)	0.81
P2Y12 inhibitor	51 (78.5%)	47 (72.3%)	0.41
Anticoagulation	20 (30.8%)	19 (29.2%)	0.84

Table 2: Angiographic characteristics of all the patients before propensity matching (n=130)

Variables	DCB (n = 65)	DES (n = 65)	P-Value
Target vessel			
Total number of lesions	65 (100.0%)	65 (100%)	---------
Multivessel disease	12 (18.5%)	14 (21.5%)	0.661
Left main coronary artery	3 (4.6%)	5 (7.7%)	0.46
Left anterior descending coronary artery	34 (49.3%)	35 (50.7%)	0.86
Left circumflex coronary artery	9 (13.8%)	10 (15.4%)	0.84
Right coronary artery	24 (36.9%)	18 (27.7%)	0.26
Bifurcation	11 (16.9%)	13 (20.0%)	0.65
Ostial lesion	6 (9.2%)	10 (15.4%)	0.28
Chronic total occlusion	2 (3.1%)	5 (7.7%)	0.24
Lesion length (mm)	17.90 (1.4)	20.04 (3.1)	0.00
Minimal lumen diameter (mm)	0.70 (0.10)	0.68 (0.09)	0.39
Reference vessel diameter (mm)	2.57(0.19)	2.62 (0.18)	0.10
Diameter stenosis (%)	50 (76.9%)	51 (78.5%)	0.83

Table 3: Procedural characteristics of all the patients before propensity matching (n=130)

Variables	DCB (n = 65)	DES (n = 65)	P-Value
Devices/procedure			
Predilatation	62 (95.4%)	57 (87.7%)	0.11
Scoring/cutting balloon	47 (72.3%)	16 (24.6%)	0.00
Non-compliant balloon	16 (24.6%)	25 (38.5%)	0.08
Diameter of DCB/DES (mm)	2.61 (0.10)	2.67(0.13)	0.004
Length of DCB/DES (mm)	18.90 (.82)	21.2 (2.72)	0.00
Intravascular ultrasound use	50 (76.9%)	53 (81.5%)	0.51
OCT use	14 (21.5%)	12 (18.5%)	0.66
Maximal pressure (atm)	12.80 (0.97)	13.33 (1.36)	0.01
Post-diameter stenosis (%)	8 (12.3%)	9 (13.8%)	0.79
Follow-up angiography (%)	54 (83.1%)	49 (75.4%)	0.28
Follow-up (days)	887.49 (7.1)	863.35 (26.5)	0.00

Discussion

The present study was conducted in our setup to compare the clinical outcomes of Drug-Coated Balloon (DCB) use for treating Stent Edge Restenosis (SER) with New-Generation Drug-Eluting Stent (DES) implantation. This study showed that the results and outcomes of DCB in treating SER are similar to those of DES. Multiple studies have pointed out that drug-coated balloons (DCB) exhibit effectiveness and safety similar to drug-eluting stents (DES) in the context of in-stent restenosis (ISR) (Cutlip et al., 2007; Jensen et al., 2018). The current study further illustrates the applicability of drug-coated balloons (DCB) in the case of patients with lesions categorized as small vessel disease (SVD). Specifically, mechanical damage or movement of the stent's edge segment can lead to the development of neointimal hyperplasia. Stent under expansion and remaining plaque also represent risk factors for stent edge restenosis (SER) (Gogas et al., 2013). Therefore, DCB angioplasty is a suitable approach for addressing SER since it has been documented to mitigate neointimal hyperplasia and unfavorable vessel remodeling (Jeger et al., 2020a). The release of anti-proliferative medications from drug-coated balloons (DCB) impedes the growth of neointima, potentially resulting in a decrease in stent edge restenosis (SER). Furthermore, DCB therapy has exhibited further beneficial effects, such as reducing plaque, promoting healing responses, and encouraging favorable vessel remodeling (Kang et al., 2013; Kleber et al., 2015). These impacts can counteract adverse remodeling; nevertheless, it has been documented that DCB treatment is comparatively less efficacious in addressing in-stent restenosis (ISR) within drug-eluting stents (DES) compared to bare metal stents (Funayama et al., 2021; Zhu et al., 2021). In the present study, the clinical outcomes observed in the DCB group closely resembled those in the DES group. Numerous potential factors contributed to the favorable results achieved with DCB in addressing stent edge restenosis (SER). One potential explanation lies in the utilization of imaging techniques during the procedure. Indeed, all patients in this study underwent assessments using imaging modalities, such as intravascular ultrasound or OCT. We use these imaging methods to evaluate lesions before and after DES implantation or before DCB angioplasty. Furthermore, calcified lesions are a recognized risk factor for target lesion revascularization (TLR) following DCB treatment (Peng et al., 2020). Nevertheless, it is widely recognized that attaining thorough plaque coverage with drug-eluting stents (DES) is essential, ensuring that the stent's edge section is positioned within a vessel with minimal plaque and calcification (Cortese et al., 2018). These measures are essential for minimizing in-stent restenosis (ISR) and thrombosis post-DES implantation. Nevertheless, despite these precautions, stent edge restenosis (SER) can still occur due to stent under expansion or calcification. In such instances, high-pressure balloons prove more effective than DCB, as DCB lacks the capability for high-pressure ballooning. Suppose an imaging device detects stent under expansion in stent edge restenosis (SER) cases. In that case, it is more probable that pre-dilatation will be employed using a high-pressure balloon to ensure sufficient expansion before either DES implantation or DCB angioplasty. As a result, suitable pre-dilatation was conducted for lesions presenting stent malapposition, stent under expansion, or calcified lesions. Therefore, imaging techniques prove valuable in elucidating the mechanisms underlying SER and enhancing the chances of a successful percutaneous coronary intervention (PCI). Utilizing a scoring balloon for pre-dilatation has the potential to amplify the advantageous outcomes of DCB. Kufner et al. documented that scoring balloons for pre-dilatation before DCB angioplasty effectively reduced the incidence of restenosis following DCB treatment (Costa et al., 2008). Scoring balloons can achieve significant lumen expansion while mitigating the risk of detrimental dissection following ballooning. Additionally, the disruptions caused by the scoring balloon in the plaque and vessel may enhance the accelerated delivery of drugs (Kufner et al., 2017). In our research, scoring balloons were commonly employed to prepare lesions in the DCB group. Consequently, these factors might have played a role in the positive results observed with DCB treatment for stent edge restenosis (SER), which is on par with the outcomes seen with the latest drug-eluting stents (DES).

Similarly, long stent implantations have been linked to an elevated risk of periprocedural myocardial infarction (MI) and stent thrombosis (Coughlan et al., 2022; Serruys et al., 2002). Minimizing the overlap of drug-eluting stents (DES) and the number of DES implantations is crucial to mitigate these adverse clinical events. Due to these considerations, drug-coated balloons (DCB) are a valuable choice for treating stent edge restenosis (SER).

Conclusion

It was concluded that following propensity score matching (PSM), the incidence of target vessel revascularization (TVR) in individuals undergoing DCB treatment for stent edge restenosis (SER) was similar to that observed in individuals treated with the latest-generation drug-eluting stents (DES). Moreover, the extended-term outcomes of DCB treatment, encompassing measures such as overall mortality, major adverse cardiovascular events (MACE), and target lesion revascularization (TLR), were similar to those seen in DES therapy. As a result, DCB stands out as an essential treatment choice for individuals with SER.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department Concerned.
Consent for publication
Approved
Funding
Not applicable

Conflict of interest

The authors declared an absence of conflict of interest.

References

Byrne, R. A., Joner, M., and Kastrati, A. (2015). Stent thrombosis and restenosis: what have we learned and where are we going? The Andreas Grüntzig Lecture ESC 2014. *European heart journal* **36**, 3320-3331.

Cortese, B., D'Ascenzo, F., Fetiveau, R., Balian, V., Blengino, S., Fineschi, M., Rogacka, R., Lettieri, C., Pavei, A., and D'Amico, M. (2018). Treatment of coronary artery disease with a new-generation drug-coated balloon: final results of the Italian Elutax SV rEgistry-DCB-RISE. *Journal of Cardiovascular Medicine* **19**, 247-252.

Cortese, B., Di Palma, G., Guimaraes, M. G., Piraino, D., Orrego, P. S., Buccheri, D., Rivero, F., Perotto, A., Zambelli, G., and Alfonso, F. (2020). Drug-coated balloon versus drug-eluting stent for small coronary vessel disease: PICCOLETO II randomized clinical trial. *Cardiovascular Interventions* **13**, 2840-2849.

Costa, M. A., Angiolillo, D. J., Tannenbaum, M., Driesman, M., Chu, A., Patterson, J., Kuehl, W., Battaglia, J., Dabbons, S., and Shamoon, F. (2008). Impact of stent deployment procedural factors on long-term effectiveness and safety of sirolimus-eluting stents (final results of the multicenter prospective STLLR trial). *The American journal of cardiology* **101**, 1704-1711.

Coughlan, J., Aytekin, A., Koch, T., Wiebe, J., Lenz, T., Cassese, S., Joner, M., Koppara, T., Xhepa, E., and Ibrahim, T. (2022). Long-term clinical outcomes after drug eluting stent implantation with and without stent overlap. *Catheterization and Cardiovascular Interventions* **99**, 541-551.

Cutlip, D. E., Windecker, S., Mehran, R., Boam, A., Cohen, D. J., van Es, G.-A., Steg, P. G., Morel, M.-a., Mauri, L., and Vranckx, P. (2007). Special Reports.

Funayama, N., Kayanuma, K., Sunaga, D., and Yamamoto, T. (2021). Serial assessment of de novo coronary lesions after drug-coated balloon treatment analyzed by intravascular ultrasound: A comparison between acute coronary syndrome and stable angina pectoris. *International Journal of Cardiology* **330**, 35-40.

Giacoppo, D., Alfonso, F., Xu, B., Claessen, B. E., Adriaenssens, T., Jensen, C., Pérez-Vizcayno, M. J., Kang, D.-Y., Degenhardt, R., and Pleva, L. (2020). Drug-coated balloon angioplasty versus drug-eluting stent implantation in patients with coronary stent restenosis. *Journal of the American College of Cardiology* **75**, 2664-2678.

Gogas, B. D., Garcia-Garcia, H. M., Onuma, Y., Muramatsu, T., Farooq, V., Bourantas, C. V., and Serruys, P. W. (2013). Edge vascular response after percutaneous coronary intervention: an intracoronary ultrasound and optical coherence tomography appraisal: from radioactive platforms to first-and second-generation drug-eluting stents and bioresorbable scaffolds. *JACC: Cardiovascular Interventions* **6**, 211-221.

Ino, Y., Kubo, T., Matsuo, Y., Yamaguchi, T., Shiono, Y., Shimamura, K., Katayama, Y., Nakamura, T., Aoki, H., and Taruya, A. (2016). Optical coherence tomography predictors for edge restenosis after everolimus-eluting stent implantation. *Circulation: Cardiovascular Interventions* **9**, e004231.

Jeger, R. V., Eccleshall, S., Wan Ahmad, W. A., Ge, J., Poerner, T. C., Shin, E.-S., Alfonso, F., Latib, A., Ong, P. J., and Rissanen, T. T. (2020a). Drug-coated balloons for coronary artery disease: third report of the international DCB consensus group. *Cardiovascular Interventions* **13**, 1391-1402.

Jeger, R. V., Farah, A., Ohlow, M.-A., Mangner, N., Möbius-Winkler, S., Weilenmann, D., Woehrle, J., Stachel, G., Markovic, S., and Leibundgut, G. (2020b). Long-term efficacy and safety of drug-coated balloons versus drug-eluting stents for small coronary artery disease (BASKET-SMALL 2): 3-year follow-up of a randomised, non-inferiority trial. *The Lancet* **396**, 1504-1510.

Jensen, C. J., Richardt, G., Tölg, R., Erglis, A., Skurk, C., Jung, W., Neumann, F.-J., Stangl, K., Brachmann, J., and Fischer, D. (2018). Angiographic and clinical performance of a paclitaxel-coated balloon compared to a second-generation sirolimus-eluting stent in patients with in-stent restenosis: the BIOLUX randomised controlled trial. *Eurointervention: Journal of Europcr in Collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology* **14**, 1096-1103.

Jimba, T., Ikutomi, M., Tsukamoto, A., Matsushita, M., and Yamasaki, M. (2021). Effect of hinge motion on stent edge-related restenosis after right coronary artery treatment in the current drug-eluting stent era. *Circulation Journal* **85**, 1959-1968.

Kang, S.-J., Cho, Y.-R., Park, G.-M., Ahn, J.-M., Kim, W.-J., Lee, J.-Y., Park, D.-W., Lee, S.-W., Kim, Y.-H., and Lee, C. W. (2013). Intravascular ultrasound predictors for edge restenosis after newer generation drug-eluting stent implantation. *The American Journal of Cardiology* **111**, 1408-1414.

Kim, Y. G., Oh, I.-Y., Kwon, Y.-W., Han, J.-K., Yang, H.-M., Park, K.-W., Lee, H.-Y., Kang, H.-J., Koo, B.-K., and Kim, H.-S. (2013). Mechanism of Edge Restenosis After Drug-Eluting Stent Implantation–Angulation at the Edge and Mechanical Properties of the Stent–. *Circulation Journal* **77**, 2928-2935.

Kitahara, H., Okada, K., Kimura, T., Yock, P. G., Lansky, A. J., Popma, J. J., Yeung, A. C., Fitzgerald, P. J., and Honda, Y. (2017). Impact of stent size selection on acute and long-term outcomes after drug-eluting stent implantation in de novo coronary lesions. *Circulation: Cardiovascular Interventions* **10**, e004795.

Kleber, F. X., Schulz, A., Waliszewski, M., Hauschild, T., Böhm, M., Dietz, U., Cremers, B., Scheller, B., and Clever, Y. P. (2015). Local paclitaxel induces late lumen enlargement in coronary arteries after balloon angioplasty. *Clinical Research in Cardiology* **104**, 217-225.

Kokkinidis, D. G., Prouse, A. F., Avner, S. J., Lee, J. M., Waldo, S. W., and Armstrong, E. J. (2018). Second-generation drug-eluting stents versus drug-coated balloons for the treatment of coronary in-stent restenosis: A systematic review and meta-analysis. *Catheterization and Cardiovascular Interventions* **92**, 285-299.

Kufner, S., Joner, M., Schneider, S., Tölg, R., Zrenner, B., Repp, J., Starkmann, A., Xhepa, E., Ibrahim, T., and Cassese, S. (2017). Neointimal modification with scoring balloon and efficacy of drug-coated balloon therapy in patients with restenosis in drug-eluting coronary stents: a randomized controlled trial. *JACC: Cardiovascular Interventions* **10**, 1332-1340.

Lin, T.-C., Huang, C.-Y., Chen, P.-L., Lee, C.-Y., Shih, C.-C., and Chen, I.-M. (2018). Edge stenosis after covered stenting for long superficial femoral artery occlusive disease: risk factor analysis and prevention with drug-coated balloon angioplasty. *Journal of Endovascular Therapy* **25**, 313-319.

Peng, N., Liu, W., Li, Z., Wei, J., Chen, X., Wang, W., and Lin, H. (2020). Drug-coated balloons versus everolimus-eluting stents in patients with in-stent restenosis: a pair-wise meta-analysis of randomized trials. *Cardiovascular therapeutics* **2020**.

Serruys, P. W., Foley, D. P., Suttorp, M.-J., Rensing, B. J., Suryapranata, H., Materne, P., van den Bos, A., Benit, E., Anzuini, A., and Rutsch, W. (2002). A randomized

comparison of the value of additional stenting after optimal balloon angioplasty for long coronary lesions: final results of the additional value of NIR stents for treatment of long coronary lesions (ADVANCE) study. *Journal of the American College of Cardiology* **39**, 393-399.

Song, C.-x., Zhou, C., Hou, W., Yin, Y., Lu, S., Liu, G., Duan, C., Li, M., and Zhang, H. (2020). Drug-eluting balloons versus drug-eluting stents for small vessel coronary artery disease: a meta-analysis. *Coronary Artery Disease* **31**, 199-205.

Tamez, H., Secemsky, E. A., Valsdottir, L. R., Moussa, I. D., Song, Y., Simonton, C. A., Gibson, C. M., Popma, J. J., and Yeh, R. W. (2021). Long-term outcomes of percutaneous coronary intervention for in-stent restenosis among Medicare beneficiaries. *Eurointervention: Journal of Europcr in Collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology* **17**, e380-e387.

Ullrich, H., Olschewski, M., Muenzel, T., and Gori, T. (2021). Coronary in-stent restenosis: predictors and treatment. *Deutsches Ärzteblatt International* **118**, 637.

Zhang, D.-M., and Chen, S. (2020). In-stent restenosis and a drug-coated balloon: insights from a clinical therapeutic strategy on coronary artery diseases. *Cardiology Research and Practice* **2020**.

Zhu, Y., Liu, K., Kong, X., Nan, J., Gao, A., Liu, Y., Han, H., Li, H., Zhu, H., and Zhang, J. (2021). Comparison of drug-coated balloon angioplasty vs. drug-eluting stent implantation for drug-eluting stent restenosis in the routine clinical practice: a meta-analysis of randomized controlled trials. *Frontiers in Cardiovascular Medicine* **8**, 766088.