

Percutaneous treatment of coronary artery disease

Zdravljenje koronarne bolezni s perkutanimi intervencijami

Igor Kranjec

This issue of the Slovenian Medical Journal (Zdravniški Vestnik – ZV) includes a review article on percutaneous coronary interventions (PCI) (1) in which the authors describe the implementation of PCI using ordinary dilated balloons (POBA), drug-eluting balloons (DEB), bare metal stents (BMS), drug-eluting stents, and bioresorbable scaffolds (BRS). The topic is important for cardiologists, so most readers of the Medical Journal may benefit from a more general editorial.

Cardiovascular diseases, especially coronary heart disease (CHD), remain a difficult-to-manage health problem despite advances in medicine and favourable epidemiological shifts. The prevalence of CHD in the European Union in 2015 was 13.2 million, mortality 0.9 million, disability caused 13.2 million lost years, and treatment cost €59 trillion (2). Annual mortality was lowest in chronic CHD (1.2–2.4%) and much higher in acute transmural (STEMI, 9%) or nontransmural myocardial infarction (NSTEMI, 11.6%) (3,4). The treatment of such a vulnerable population must be proven to be effective and comprehensive. Optimal non-invasive treatment consisting of lifestyle changes,

risk factor control, LDL cholesterol lowering drugs, antithrombotic therapy, and anti-ischaemic drugs are always beneficial (3). These measures slow down the process of atherosclerosis, prevent ischaemic complications and relieve symptoms. Only strict control of risk factors contributes to a reduction in mortality by half, and other drugs and coronary revascularization contribute to the other half (4).

Coronary revascularization is beneficial to carefully selected patients. In chronic CHD, despite some concerns (6,7), it is used in persistent symptoms, unfavourable coronary anatomy (multivessel CHD, narrowing of the trunk of the left coronary artery or the proximal left anterior descending artery), extensive myocardial ischaemia (> 10%) or severe left ventricular systolic dysfunction (\leq 35%) (3). In STEMI, PCI is the method of choice in the first 12 hours after an acute event (8). In NSTEMI, the decision to revascularize is more complex and also depends on the degree of ischaemic risk and associated diseases (9).

The purpose of coronary revascularization is to bridge or remove critical constrictions. It can be

Department of Cardiology, Division of Internal Medicine, University Medical Centre Ljubljana, Ljubljana, Slovenia

Correspondence / Korespondenca: Igor Kranjec, e: igor.kranjec@gmail.com

Key words: percutaneous coronary intervention; stent; balloon angioplasty; coronary disease; history

Ključne besede: perkutana koronarna intervencija; žilna opornica; balonska angioplastika; koronarna bolezen; zgodovina

Received / Prispelo: 9. 10. 2020 | **Accepted / Sprejeto:** 11. 10. 2020

Cite as / Citirajte kot: Kranjec I. Percutaneous treatment of coronary artery disease. Zdrav Vestn. 2021;90(7–8):365–8. DOI: <https://doi.org/10.6016/ZdravVestn.3246>



Copyright (c) 2021 Slovenian Medical Journal. This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

performed surgically (coronary artery bypass grafting, CABG) or by PCI. CABG was first performed by Robert Goetz and Michael Rohman in the Bronx in 1960, and PCI was first performed by Andreas Grüntzig in Zurich in 1977. CABG uses arterial and venous bypasses and is the reference method for revascularization, but is more invasive and more difficult for patients to access. Therefore, patients like to opt for PCI.

PCI has undergone major changes over the last 40 years, overcoming many obstacles while opening up new challenges. Interventional cardiologists initially used the POBA technique: the dilatation balloon was brought to the narrowing site with a guide wire, inflated to ~10 atmospheres, and emptied after a few times 10 seconds. Thus, they achieved a beautiful angiographic result while at the same time causing extensive vascular damage. The balloon dilatation, namely, achieves the expansion of vascular lumen at the expense of tearing the diseased intima and media and stretching the “healthy” wall (10). This resulted in frequent sudden vascular obstruction (2–6%) and subsequent recurrent stenosis (RST, 30–50%) (10). POBA therefore took place under surgical precautions.

In this atmosphere, the introduction of vascular stents was a real relief. The first BMSs were made of stainless steel, mesh, spiral, or tubular structure, and were self-expanding or imprinted into vascular stenosis with dilated balloons. They were foreign to the organism, so a violent thrombotic and inflammatory response followed. Fortunately, the proper implantation technique using high pressures and aggressive antiplatelet therapy prevented the risk of acute stent thrombosis. PCI has become safe, but the frequency of RST was too high (22–32%) despite the BMS production improvements (11).

RST in BMS causes myointimal proliferation, so the use of antiproliferative drugs was a logical step. First-generation DESs were still made of stainless steel and had a polymer coating rich with cytostatic sirolimus or paclitaxel. The large Scandinavian SCAAR registry reported that the frequency of RST two years after implantation decreased by 38% compared to BMS (12). However, the cytostatics used were too potent, as they inhibited the endothelialisation of metal stents and, together with tissue hypersensitivity to the polymer, led to the dangerous occurrence of late stent thrombosis (2.6%), myocardial infarction or sudden cardiac death (4.9%) (13).

The desire for greater safety has led to many changes in the DES structure. Stainless steel has been replaced by cobalt and chromium, polymers have become more

inert, degradable or non-existent, and sirolimus and paclitaxel have been replaced by newer drugs (e.g. everolimus, zotarolimus, novolimus). The second-generation DES reduced the incidence of late thrombosis by 52% compared to BMS and by 58% compared to the first-generation DES (14).

The ideal vascular stent provides mechanical support and antiproliferative drug one year after insertion, then completely degrades, restores the normal vasomotor function and eliminates the focus for subsequent ischaemic complications. Therefore, much was expected of BRS. They consisted of poly-L-lactic acid or magnesium, polymer and antiproliferative drug. However, due to rapid degradation, their radial force was weak and the incidence of thrombosis one year after insertion was almost four times higher compared to DES (15). Therefore, BRS had to be withdrawn from the market in 2017. The recent ABSORB IV study demonstrated, with an optimal implantation technique, their equivalence compared to DES in terms of clinical outcomes in the first year (16), but the future of BRS remains uncertain.

And only briefly about the use of DEB in clinical practice: scientific evidence limits them only to the treatment of RST in previously placed stents (15).

In this paragraph, we present the history of PCI and compare the first implementations of individual techniques around the world and in Slovenia (Figure 1). We tried to give recognition to the experts who paved the way for PCI in pioneering conditions, by stating their names. The first PCI (POBA) was performed by Andreas Grüntzig in Zurich in 1977. In Slovenia, the first POBA was electively carried out by Ivo Obrez and Miran Kenda in 1985 and in STEMI by Dušan Pavčnik and Igor Kranjec in 1989. The first coronary vascular stent (BMS) was inserted by Jacques Puel in Toulouse and Ulrich Sigwart in Lausanne in 1986. In our country, the first BMS was electively inserted by Silvio Klugmann in 1995 (Figure 2 A, B), in an emergency situation by Matjaž Šinkovec in 1998, and in STEMI Radovan Starc in 1998. A continuous service for the implementation of PCI in emergency situations was established at the University Medical Centre in Ljubljana in 2000. The first DES was inserted by J. Eduardo Sousa in Sao Paulo in 1999. In Slovenia, DES was electively inserted by Darko Zorman in 2003, and in STEMI by Igor Zupan in 2004. The first BRS was inserted by Hideo Tamai and Keiji Igaki in Kyoto in 1998. In our country, the first BRS was electively inserted by Darko Zorman in 2012, and at STEMA by Matjaž Bunc in 2013.

Further development of PCI is difficult to predict.

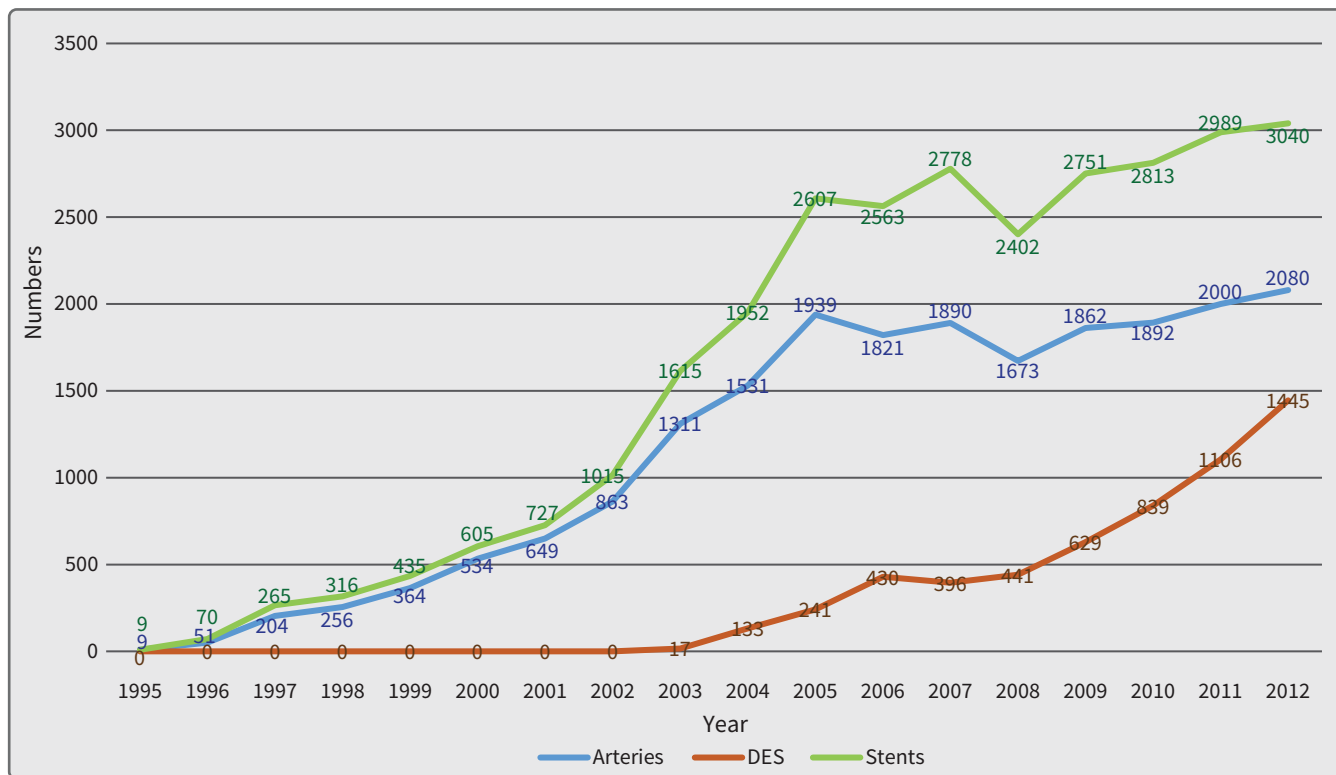


Figure 1: Demonstration of percutaneous coronary interventions (PCI) in the catheter laboratory of the Clinical Department of Cardiology, University Medical Centre Ljubljana, for the period 1995–2012. It shows the use of all stents, drug-eluting stents (DES) and the number of stented arteries.

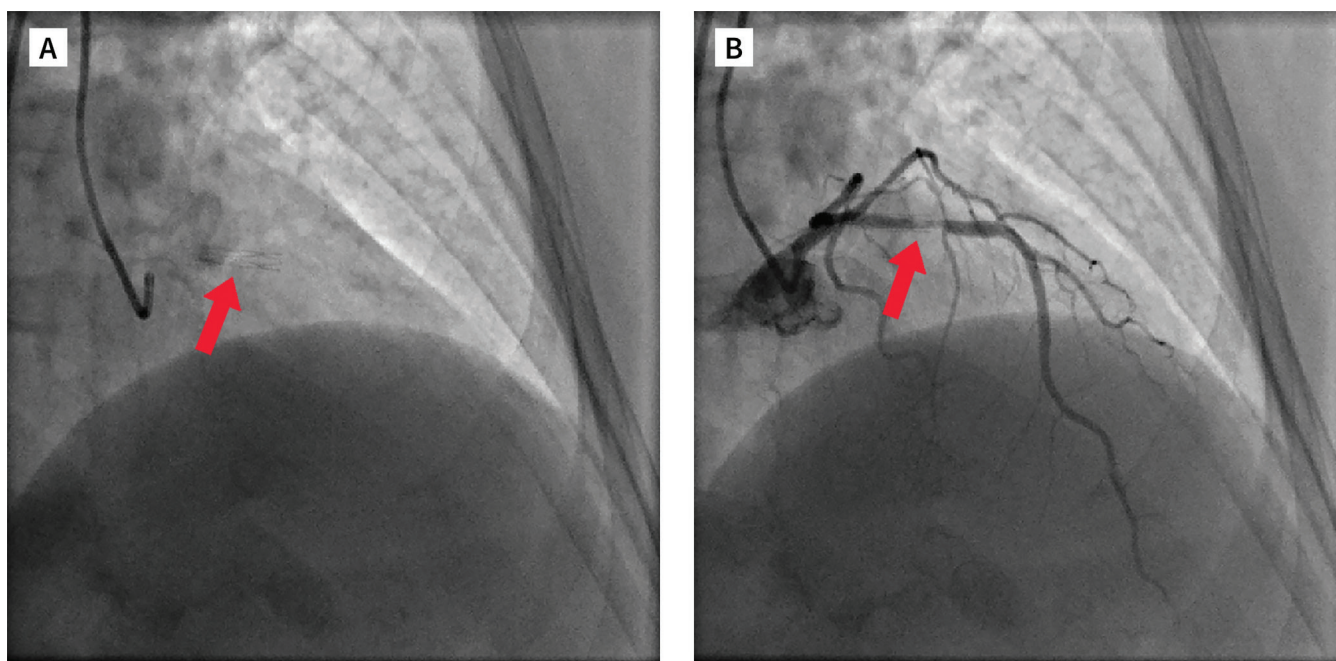


Figure 2: A. Angiographic image of the first coronary stent (AVE inc. Santa Roza, CA) inserted in the Ljubljana catheter laboratory in 1995. B. Angiographic image of restenosis in the same stent 14 years later.

Most likely, however, it will be a continuation of modern good practice, which has withstood many challenges. We anticipate that patients will be treated individually and holistically, with the clinical presentation of the disease and the general condition of the patient playing the most important role. The technique and extent of PCI will be decisively influenced by imaging and functional examinations before and during the procedure (e.g. CT angiography, IVUS/OCT, coronary blood flow measurements). Entry into the vascular space will be easy and repeatable (e.g. radial artery), the devices used will be miniaturized. The standard PCI will be based on the insertion of DES of newer generations. The role of the BRS, however, is currently unclear. Additional

devices (e.g. rotablation, orbital atherectomy, lithotripsy) and intervention strategy (e.g. antegrade and retrograde approach, thrombus removal) will be used depending on the anatomical complexity of the coronary lesions. Advances in vascular stents (e.g. stent thickness) will allow for the shortest possible aggressive antiplatelet therapy and thus reduce the number of serious bleeds. Good regional organization of catheter laboratories will allow urgent patients immediate access to optimal treatment. Last but not least, online links between learning centres will ensure the transfer of modern expertise and offer direct assistance during interventions.

References

1. Žlahtič T, Vitez L, Bunc M. Preteklost, sedanjost, prihodnost: razvoj perkutane koronarne intervencije. *Zdrav Vestn.* 2021;90(7–8):420–31. DOI: [10.6016/ZdravVestn.3084](https://doi.org/10.6016/ZdravVestn.3084)
2. European Cardiovascular Disease statistics 2017. Brussels: European Heart Network; 2017. Available from: <https://ehnheart.org/cvd-statistics/cvd-statistics-2017.html>.
3. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, et al.; ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J.* 2020;41(3):407–77. DOI: [10.1093/eurheartj/ehz425](https://doi.org/10.1093/eurheartj/ehz425) PMID: [31504439](https://pubmed.ncbi.nlm.nih.gov/31504439/)
4. Montalescot G, Dallongeville J, Van Belle E, Rouanet S, Baulac C, Degrandart A, et al.; OPERA Investigators. STEMI and NSTEMI: are they so different? 1 year outcomes in acute myocardial infarction as defined by the ESC/ACC definition (the OPERA registry). *Eur Heart J.* 2007;28(12):1409–17. DOI: [10.1093/eurheartj/ehm031](https://doi.org/10.1093/eurheartj/ehm031) PMID: [17412730](https://pubmed.ncbi.nlm.nih.gov/17412730/)
5. Simoons ML, Windecker S. Controversies in cardiovascular medicine: Chronic stable coronary artery disease: drugs vs. revascularization. *Eur Heart J.* 2010;31(5):530–41. DOI: [10.1093/eurheartj/ehp605](https://doi.org/10.1093/eurheartj/ehp605) PMID: [20106842](https://pubmed.ncbi.nlm.nih.gov/20106842/)
6. Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, et al.; COURAGE Trial Research Group. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med.* 2007;356(15):1503–16. DOI: [10.1056/NEJMoa070829](https://doi.org/10.1056/NEJMoa070829) PMID: [17387127](https://pubmed.ncbi.nlm.nih.gov/17387127/)
7. Al-Lamee R, Thompson D, Dehbi HM, Sen S, Tang K, Davies J, et al.; ORBITA investigators. Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial. *Lancet.* 2018;391(10115):31–40. DOI: [10.1016/S0140-6736\(17\)32714-9](https://doi.org/10.1016/S0140-6736(17)32714-9) PMID: [29103656](https://pubmed.ncbi.nlm.nih.gov/29103656/)
8. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al.; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 2018;39(2):119–77. DOI: [10.1093/eurheartj/ehx393](https://doi.org/10.1093/eurheartj/ehx393) PMID: [28886621](https://pubmed.ncbi.nlm.nih.gov/28886621/)
9. Collet JP, Thiele H, Barbato E, Barthelémy O, Bauersachs J, Bhatt DL, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *European Heart Journal.* 2020;00:1–79. DOI: [10.1093/eurheartj/ehaa575](https://doi.org/10.1093/eurheartj/ehaa575) PMID: [32860058](https://pubmed.ncbi.nlm.nih.gov/32860058/)
10. Waller BF, Orr CM, Pinkerton CA, VanTassel JW, Pinto RP. Morphologic observations late after coronary balloon angioplasty: mechanisms of acute injury and relationship to restenosis. *Radiology.* 1990;174(3 Pt 2):961–7. DOI: [10.1148/radiology.174.3.174-3-961](https://doi.org/10.1148/radiology.174.3.174-3-961) PMID: [2406792](https://pubmed.ncbi.nlm.nih.gov/2406792/)
11. Hong MK. Restenosis following coronary angioplasty: current status. *Korean J Intern Med (Korean Assoc Intern Med).* 2001;16(2):51–5. DOI: [10.3904/kjim.2001.16.2.51](https://doi.org/10.3904/kjim.2001.16.2.51) PMID: [11590901](https://pubmed.ncbi.nlm.nih.gov/11590901/)
12. James SK, Stenestrand U, Lindbäck J, Carlsson J, Scherstén F, Nilsson T, et al.; SCAAR Study Group. Long-term safety and efficacy of drug-eluting versus bare-metal stents in Sweden. *N Engl J Med.* 2009;360(19):1933–45. DOI: [10.1056/NEJMoa0809902](https://doi.org/10.1056/NEJMoa0809902) PMID: [19420363](https://pubmed.ncbi.nlm.nih.gov/19420363/)
13. Camenzind E, Steg PG, Wijns W. Stent thrombosis late after implantation of first-generation drug-eluting stents: a cause for concern. *Circulation.* 2007;115(11):1440–55. DOI: [10.1161/CIRCULATIONAHA.106.666800](https://doi.org/10.1161/CIRCULATIONAHA.106.666800) PMID: [17344324](https://pubmed.ncbi.nlm.nih.gov/17344324/)
14. Palmerini T, Benedetto U, Biondi-Zoccai G, Della Riva D, Bacchi-Reggiani L, Smits PC, et al. Long-term safety and efficacy of drug-eluting and bare-metal stents. *J Am Coll Cardiol.* 2015;65(23):2496–507. DOI: [10.1016/j.jacc.2015.04.017](https://doi.org/10.1016/j.jacc.2015.04.017) PMID: [26065988](https://pubmed.ncbi.nlm.nih.gov/26065988/)
15. Tomberli B, Mattesini A, Baldereschi GI, Di Mario C. A Brief History of Coronary Artery Stents. *Rev Esp Cardiol (Engl Ed).* 2018;71(5):312–9. DOI: [10.1016/j.rec.2017.11.022](https://doi.org/10.1016/j.rec.2017.11.022) PMID: [29361499](https://pubmed.ncbi.nlm.nih.gov/29361499/)
16. Stone GW, Ellis SG, Gori T, Metzger DC, Stein B, Erickson M, et al.; ABSORB IV Investigators. Blinded outcomes and angina assessment of coronary bioresorbable scaffolds: 30-day and 1-year results from the ABSORB IV randomised trial. *Lancet.* 2018;392(10157):1530–40. DOI: [10.1016/S0140-6736\(18\)32283-9](https://doi.org/10.1016/S0140-6736(18)32283-9) PMID: [30266412](https://pubmed.ncbi.nlm.nih.gov/30266412/)