Bioresorbable vascular scaffolds for percutaneous treatment of chronic total coronary occlusions: a meta-analysis

Alberto Polimeni1,2†, Remzi Anadol1, Thomas Münzel1, Martin Geyer1, Salvatore De Rosa2, Ciro Indolfi2,3† and Tommaso Gori1*†

Abstract

Background: BRS represent a new approach to treating coronary artery disease. Beneficial properties of BRS regarding the restoration of vasomotility after resorption make them attractive devices in CTO revascularization. However, experience in this setting is limited.

Methods: We systematically searched Medline, Scholar, and Scopus for reports of at least 9 patients with CTO undergoing BRS implantation. Patients’ and procedural characteristics were summarized. The primary outcome of interest was target lesion revascularization (TLR). Pooled estimates were calculated using a random-effects meta-analysis. The study protocol was registered in PROSPERO (CRD42017069322).

Results: Thirteen reports for a total of 843 lesions with a median follow-up of 12 months (IQR 6–12) were included in the analysis. At short-term, the summary estimate rate of TLR was 2.6% (95% CI: 1 to 4%, I² = 0%, P = 0.887) while at mid to long-term it was 3.8% (95% CI: 2 to 6%, I² = 0%, P = 0.803). At long-term follow-up (≥12 months), the summary estimate rate of cardiac death was 1.1% (95% CI: 0 to 2%, I² = 0%, P = 0.887). The summary estimate rates of scaffold thrombosis and clinical restenosis were respectively 0.9% (95% CI: 0 to 2%, I² = 0%, P = 0.919) and 1.8% (95% CI: 0 to 4%, I² = 0%, P = 0.448). Finally, the summary estimate rate of target vessel revascularization was 6.6% (95% CI: 0 to 11%, I² = 0%, P = 0.04).

Conclusions: Implantation of BRS in a population with CTO is feasible, although further longer-term outcome studies are necessary.

Keywords: Implantation of BRS in a population with CTO is feasible, although further longer-term outcome studies are necessary.

Background

Chronic total occlusions (CTO) are present in about 20% of patients with coronary artery disease undergoing elective angiography [1]. Nevertheless, these lesions represent only a minority of the lesions treated with percutaneous coronary intervention (PCI), even if their treatment is associated with better outcome in terms of angina relief, improved left ventricular function, reduction in the rate of myocardial infarction and coronary artery bypass grafting (CABG), and potentially prolonged survival, particularly in the setting of multivessel disease when complete revascularization is achieved [2].

After successful recanalization of the vessel, stenting is mandatory, preferably with drug-eluting stents (DES), to ensure long-term vessel patency [3]. Although favorable long-term outcome data have been reported after the implantation of DES, the implantation of multiple metallic stents into coronary arteries may lead to an augmented risk of restenosis and thrombosis, impairment of vasomotion and positive remodeling and excludes the possibility of future bypass graft anastomosis within these segments [4]. In this setting, bioresorbable scaffolds (BRS) might therefore have potential advantages: avoidance of long coronary segments covered with metallic prostheses, restoration of...
endothelial function and normal vasomotor tone at least within noncalcified segments, long-term favourable vessel remodeling; finally, struts resorption preserves the possibility of further interventions by percutaneous or surgical means [5].

Conversely, there are also many limitations of BRS use in this subset of lesions: severely calcified vessels may be poorly accessible for bulky devices, and their low radial strength bear the risk of vessel recoil and underestimation of vessel size raise the risk of malapposition.

Importantly, CTO lesions were excluded in all BRS randomized controlled trials published to date [6–9], and all available evidence derives from small single-center, single-arm studies. We therefore undertook a systematic literature review and meta-analysis of studies examining the clinical outcomes of patients with chronic coronary occlusion undergoing BRS implantation.

Methods
Search strategy
Electronic searches were performed using Pubmed, Scholar, and Scopus electronic database up to June 13th, 2017. We checked the reference lists from all eligible studies to identify additional citations. The following keywords and the corresponding MeSH terms were used for search: “biodegradable vascular scaffold”, “chronic total occlusion”, “coronary artery disease”. Time of publication was not limiting criterion for our analysis. All reports including the search terms were independently screened by two investigators for relevance and eligibility (AP, SDR) and any disagreement was resolved by consensus. The study protocol was registered in PROSPERO (CRD42017069322).

Study selection
Inclusion criteria: 1) patients with at least one coronary chronic total occlusion 2) reports of a minimum of 9 patients with a follow-up at least of 1 month; 3) original articles reporting at least one of these outcomes: target lesion revascularization (TLR), target vessel revascularization (TVR), scaffold thrombosis (ScT), scaffold restenosis (ScR), cardiac death and 4) reports written in English language.

Exclusion criteria: 1) duplicate publication 2) pre-specified endpoint 3) measure not specified. If duplicate studies were identified, only the most exhaustive and recent reports were retained.

Data extraction
Baseline characteristics as well as numbers of events were extracted from the single studies, through scanning of the full article by two independent reviewers (AP, SDR). Divergences were resolved by consensus.

The following data were abstracted: year of publication, location, number of study patients, study design, clinical outcome data, baseline patients’ characteristics, and procedural characteristics.

Study endpoints
TLR was the primary outcome of interest. Secondary outcomes were TVR, ScT, clinical ScR, cardiac death.

Statistical analysis
Categorical variables are reported as numbers and percentage, and continuous variables are reported as mean ± SD or median ± IQR. Random effects meta-analysis was conducted in all analyses using the Metaprop command, which allows computation of 95% confidence intervals (CIs) using the score statistic and the exact binomial method and incorporates the Freeman-Tukey double arcsine transformation of proportions [10]. Heterogeneity among studies was assessed with the I² statistic. The effect of study-level covariates on the rate of TLR, ScT and ScR was explored with a meta-regression analysis by using the metareg command (Additional file 1). All analyses were performed with OpenMetaAnalyst software version 0.15 [11] and Stata statistical software version 13 (StataCorp LP, College Station, Texas).

Results
Search results
Our search retrieved a total of 304 entries, which were reduced to 59 studies after an initial pre-screening. 43 studies were then excluded for one of the following reasons: a) they were not related to our research question b) they weren't original articles. In the assessment of eligibility 1 additional study was excluded because as it is limited to in-hospital outcomes [12]. Finally, a total of 13 studies [13–25] with a median follow-up of 12 months (IQR 6–12) were available for the analysis including 843 lesions. The study selection procedure is reported in detail in Fig. 1.

Study characteristics
Table 1 summarizes the patients’ most relevant baseline characteristics for each study.

Across studies, patients were predominantly male and had a mean left ventricle ejection more than 50% while the percentages of patients with diabetes (3.3–51.2%), smoking (8–77.8%) and prior-PCI were variable (13.3–56.1%).

Lesion and procedural details are provided in Table 2. The percentage of lesion with moderate/severe calcification (0–70.5%) and that of lesions with a J-CTO score more or equal than 2 (26–100%) were variable while the percentage of post-dilation was almost similar and more than 69.6% in all the studies with the exception of the study by Saad et al. 2016 (25.7%).
Meta-analysis
The primary analysis on the composite endpoint of TLR both at short-term (< 6 months) and mid to long-term (> 11 months) term follow-up including all results of the studies is presented in Fig. 2. At short-term, the summary estimate rate of TLR was 2.6% (95% CI: 1 to 4%, $I^2 = 0\%$, $P = 0.887$, Fig. 2a) while at mid to long-term was 3.8% (95% CI: 2 to 6%, $I^2 = 0\%$, $P = 0.803$, Fig. 2b).

Secondary endpoints are reported in Fig. 2c. At mid to long-term follow-up, the summary estimate rate of cardiac death was 1.1% (95% CI: 0 to 2%, $I^2 = 0\%$, $P = 0.887$, Fig. 2c, first row). The summary estimate rates of scaffold thrombosis and clinical restenosis were respectively 0.9% (95% CI: 0 to 2%, $I^2 = 0\%$, $P = 0.919$, Fig. 2c, second row) and 1.8% (95% CI: 0 to 4%, $I^2 = 0\%$, $P = 0.448$, Fig. 2c, third row). Finally, the summary estimate rate of target vessel revascularization was 6.6% (95% CI: 0 to 11%, $I^2 = 0\%$, $P = 0.04$, Fig. 2c, fourth row).

Meta-regression analysis
Given the differences between Japan-Chronic Total Occlusion (J-CTO) score between the studies, we used the percentage of interventional procedures with J-CTO ≥ 2 in every single study as a moderator in a meta-regression analysis with the effect size of all endpoints evaluated. Probably due to small sample size, we found only no significant interactions across the studies between J-CTO score ≥ 2 on the incidence of TLR ($p = 0.21$), ISR ($p = 0.11$), ScT ($p = 0.935$). Results of meta-regression analyses are displayed in Additional file 1.

Discussion
Although the studies leading to their CE marking were mostly based on the analysis of outcomes after treatment of simple lesions, BRS have been used since their introduction in increasingly complex ones. In these settings, including thrombotic, ostial or bifurcation lesions or chronic total occlusions, the potential benefits of vascular resorption...
### Table 1 Baseline patient’s characteristics

| Characteristic      | Abellas et al. 2017 | Azzalini et al. 2016 | Fam et al. 2017 | Goktekin et al. 2015 | Kugler et al. 2017 | Lesiak et al. 2016 | Mitomo et al. 2016 | Ozeda et al. 2015 | Ozel et al. 2016 | Saad et al. 2016 | Vaquerizo et al. 2016 | Wiebe et al. 2015 | Yamac et al. 2017 |
|---------------------|---------------------|----------------------|-----------------|----------------------|-------------------|--------------------|--------------------|-------------------|-----------------|----------------|----------------------|----------------------|---------------------|
| Age (years)         | 59.2 ± 8.7          | 60.0 ± 9.3           | 59.40 ± 8.96    | 56.9 ± 9.4           | 60.5 ± 7.8        | 599 ± 83           | 608 ± 11.0         | 58 ± 9            | 619 ± 9.7        | 65.3 ± 109      | 61 ± 10               | 60.4 ± 9.0           | 57.8 ± 9.6          |
| Male (%)            | –                   | 89.5                 | 89.5            | 90.0                 | 85.7              | 775                | 892                | 98                | 854             | 75              | 17.1                  | 81.8                 | 78.6                |
| Hypertension (%)    | 44.4                | 65.4                 | 69.5            | 78.6                 | 64.3              | 80                 | 678                | 57                | 805             | 78.6            | –                    | 91.3                 | 80.1                |
| Diabetes (%)        | 22.2                | 34.0                 | 33.3            | 21.4                 | 14.3              | 30                 | 40                 | 33                | 51.2            | 26.3            | 20                   | 34.8                 | 3.3                 |
| Smoking (%)         | 77.8                | 24.8                 | 48.6            | 35.7                 | 57.1              | 35                 | –                  | 8                 | 34.1            | 41.5            | –                    | 47.8                 | 40                  |
| Family History (%)  | –                   | 29.6                 | 21.9            | 32.9                 | –                 | –                  | –                  | –                 | 30.8            | –              | –                    | 33.3                 |                     |
| Hyperlipidemia (%)  | 100                 | 69.9                 | 72.4            | 52.9                 | 71.4              | –                  | 615                | 64                | 463             | 50.4            | –                    | 65.2                 | 56.7                |
| Prior CABG (%)      | –                   | 2.6                  | 2.9             | 10                   | 0                 | 5                  | 62                 | –                 | 17.1            | 2.7             | –                    | –                    | 6.7                 |
| Prior PCI (%)       | –                   | 43.8                 | 46.7            | 17.1                 | –                 | 45                 | 538                | 36                | 56.1            | 39.3            | –                    | –                    | 13.3                |
| Prior stroke/TIA (%)| 0                   | 2.6                  | –               | 0                    | –                 | –                  | 308                | –                 | –               | –              | –                    | –                    | 0                   |
| CKD (%)             | –                   | 5.5                  | –               | 2                    | 7.1               | 15                 | 40.1               | –                 | 0               | –              | –                    | –                    | 0                   |
| LVEF (%)            | –                   | 53.2 ± 10.1          | –               | 51.7 ± 6.7           | –                 | 507 ± 102          | 577 ± 10.8         | 54 ± 8            | 59.8 ± 13.8      | –              | 55.7 ± 15.5          | –                    | 50.2 ± 6.4          |
| Table 2 Lesion and procedural characteristics |
|-----------------------------------------------|
|                  | Abellas et al. 2017 | Azzalini et al. 2016 | Fam et al. 2017 | Goktekin et al. 2015 | Kugler et al. 2017 | Lesiak et al. 2016 | Mtomo et al. 2016 | Ojeda et al. 2015 | Ozel et al. 2016 | Saad et al. 2016 | Vaquerizo et al. 2016 | Webe et al. 2015 | Yamac et al. 2017 |
| LAD (%)          | 22.2                | 46.4                | 41.9            | 51.4                | 20                   | 57.5               | 46.2               | 48               | 34.1               | 41.6               | –                 | 435               | 34.3               |
| LCX (%)          | 0                   | 19.0                | 12.4            | 24.3                | 67                   | 12.3               | 24                | 17               | 17                | 266               | –                 | 8.7               | 25.7               |
| RCA (%)          | 77.8                | 34.6                | 44.8            | 32.9                | 73.3                 | 35                 | 40                | 28               | 48.7               | 31.7               | 46                | 47.8               | 40                 |
| Moderate/Severe calcifications (%)            | 66.7                | 45.8                | 70.5            | 28                  | 46.7                 | 30                 | 32.3              | –                | –                 | 0                 | 34                | 652               | 22.9               |
| J-CTO score ≥ 2 | 55.5                | 42.5                | 100             | –                   | 60                   | 55                 | 64.6              | 46               | 29.2              | –                 | 26                | –                 | –                 |
| RVD (mm)        | 3.39 ± 0.22         | 3.0 ± 0.4           | 2.71 ± 0.55     | –                   | 3.24 ± 0.046         | 2.48 ± 0.33        | 2.97 ± 0.36       | 3.03 ± 0.4       | 2.8 ± 0.25        | 3.1 ± 0.5           | 2.48 ± 0.048       | –                 | 3.02 ± 0.39    |
| Mean number of BRS implanted                | 3.22                | 2.2 ± 1.1           | 2.44 ± 1.12     | 2.01 ± 1.0          | 3.2 ± 1.3            | 16 (1–4)          | 1.8 ± 0.7         | 2.6 ± 1.9        | 1.27              | 1.63              | –                 | 28 ± 1.0           | 2.3 ± 0.9         |
| Mean BRS diameter (mm)                      | 3.29 ± 0.31         | 3.2 ± 0.4           | 3.00 ± 0.31      | 3.0 ± 0.4           | –                   | 2.90 ± 0.32        | 3.0 ± 0.4         | 3.030 ± 0.38     | 2.8 ± 0.29        | 3.1 ± 0.4           | –                 | 3.1 ± 0.2          | 3.2 ± 0.4         |
| Total BRS length (mm)                       | 21.93 ± 6.45        | 51.3 ± 24.1         | 59.75 ± 25.85   | 36.5 ± 19.5         | 81.7 ± 29.1          | 42.4 ± 21.5        | 47.6 ± 19.9       | 43 ± 21          | 25.6 ± 4.2        | 26 ± 14.7          | 53 ± 23            | 648 ± 24.2         | 58.3 ± 23.3       |
| Post-dilation (%)                           | 88.9                | 90.8                | 89.5            | 100                 | 100                  | 95                 | 100               | 100             | 97.5              | 25.7              | 63                | 696               | 100               |
| Mean post-dilation Balloon diameter (mm)     | 3.45 ± 0.28         | 3.3 ± 0.4           | 3.35 ± 0.44     | 3.5 ± 0.4           | 3.3 ± 0.4            | 3.15 ± 0.35        | 3.3 ± 0.3         | –               | –                 | –                 | –                 | –                 | 3.4 ± 0.4         |
could theoretically be larger; on the other side, particularly in light of recent meta-analyses reporting inferior results compared to modern drug eluting stents in simple lesions [26, 27], this use is not based on evidence and outcomes remain to be reported.

In this study, we summarize the clinical evidence on the use of BRS for the treatment of CTOs. Our reported TLR rate of 3.8% (FU > 11 months) compares favorably with that recently reported by Stone et al. (BRS 2.7%, EES 2.3% at 1 year) in a recent meta-analysis of studies.

![Fig. 2](image.png)

Fig. 2 Random effects meta-analysis of target lesion revascularization (TLR) at short-term (panel a) and mid to long-term (panel b) follow-up. (panel c) Random effects meta-analyses of cardiac death, target vessel revascularization, scaffold thrombosis and restenosis at mid to long-term follow-up.
on the use of BRS in simple coronary lesions [28]. As well, the rates of TVR (6.6%), cardiac death (1.1%), scaffold thrombosis (0.9%), clinical scaffold restenosis (1.8%) at mid to long-term follow-up are in line with data reported in previous meta-analyses on the use of DES in CTO lesions. For instance, Yang SS et al. in a meta-analysis of 29 studies [29] reported an incidence of 1.35% of DES thrombosis in this setting at 1-year follow-up, while Colmenarez et al. reported, in another meta-analysis, a TVR rate of 11.71% at 6 to 36 months follow-up [30]. In a recent research letter, Brugaletta et al., suggested the use of ticagrelor in patients undergoing PCI of CTO with the potential to improve vascular function and to reduce TLR and symptoms [31]. Taken together, the present data appear to support the use of BRS in CTO setting.

Limitations
First, studies with BRS implantation in CTOs are limited in number and mostly single arm, observational and/or include a small sample size. Second, publication bias may have affected the findings of our meta-analysis of published reports. The lack of routine follow-up angiography in most of the studies does not allow detection of the occurrence of some outcomes like restenosis [32]. Third, although we explored the effect of covariates on the effect size, the results of the meta-regression should be carefully interpreted in view of the use of study-level covariates and overall low statistical power [33–35]. Fourth, no data are available on procedural success rates. BRS are bulkier and require a more accurate lesion preparation, which is often harder to achieve in complex lesions [36–41]. Finally, the present data reflect outcomes of BRS in selected centers with expertise in this specific setting, and any assumption of safety should be taken with caution.

Conclusions
Implantation of BRS in a population with CTO is feasible, although further longer-term outcome studies are necessary.

Additional file

Additional file 1: Metaregression analyses - The effect of study-level covariates on the rate of TLR, ScR and ScT. (PPTX 161 kb)

Abbreviations
BRS: Bioresorbable scaffolds; CABG: Coronary artery bypass grafting; CTO: Chronic total occlusions; DES: Drug-eluting stents; MACE: Major adverse cardiovascular events; MI: Myocardial infarction; PCI: Percutaneous coronary interventions; ScR: Scaffold restenosis; ScT: Scaffold thrombosis; TLR: Target-lesion revascularization; TVF: Target vessel failure; TVR: Target-vessel revascularization

Acknowledgements
None

Funding
None

Availability of data and materials
All data generated or analysed during this study are included in this published article.

Authors’ contributions
AP, SDR, and TG designed the study and acquired, analysed, and interpreted data. AP, MG and RA did the literature search and study selection procedures. TM and CI drafted the manuscript, with critical revisions for important intellectual content from all authors. All authors read and approved the final manuscript.

Ethics approval and consent to participate
Not applicable

Consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests.

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Author details
1 Kardiologie I, Zentrum für Kardiologie, University Medical Center Mainz and DZHK Standort Rhein-Main, Mainz, Germany. 2 Division of Cardiology, Department of Medical and Surgical Sciences, “Magna Graecia” University, 88100 Catanzaro, Italy. 3 URT-CNR, Department of Medicine, Consiglio Nazionale delle Ricerche of IFC, Viale Europa S/N, 88100 Catanzaro, Italy.

Received: 19 March 2018 Accepted: 12 March 2019
Published online: 15 March 2019

References
1. Galassi AR, Brilakis ES, Boukhris M, et al. Appropriateness of percutaneous revascularization of coronary chronic total occlusions: an overview. Eur Heart J. 2016;37:2692–700.
2. Jones DA, Weerackody R, Rathod K, et al. Successful recanalization of chronic total occlusions is associated with improved long-term survival. JACC Cardiovasc Interv. 2012;5:380–8.
3. Roffi M, Iglesias JF. CTO PCI in patients with diabetes mellitus: sweet perspectives. JACC Cardiovasc Interv. 2017;10:2182–4.
4. Dinesch V, Burian M. Drug-eluting stent failure: A complex scenario. Int J Cardiol. 2017;247:26.
5. Indolfi C, De Rosa S, Colombo A. Bioresorbable vascular scaffolds - basic concepts and clinical outcome. Nat Rev Cardio. 2016;13:719–29.
6. Gao R, Yang Y. Han yet al. Bioresorbable everolimus-eluting bioresorbable scaffold and an everolimus-eluting metallic stent: insights from the randomised ABSORB Japan trial. EuroIntervention. 2016;12:1000–101.
7. Onuma Y, Sotomi Y, Shiomi H, et al. Two-year clinical, angiographic, and serial optical coherence tomographic follow-up after implantation of an everolimus-eluting bioresorbable scaffold and an everolimus-eluting metallic stent: insights from the randomised ABSORB II trial. EuroIntervention. 2016;12:1102–7.
8. Chevalier B, Onuma Y, van Boven AJ, et al. Randomised comparison of a bioresorbable everolimus-eluting scaffold with a metallic everolimus-eluting stent for ischaemic heart disease caused by de novo native coronary artery lesions: the 2-year clinical outcomes of the ABSORB II trial. EuroIntervention. 2016;12:1102–7.
9. Wykryzkovska JJ, Kraap RK, Hofma SH, et al. Bioresorbable scaffolds versus metallic stents in routine PCI. N Engl J Med. 2017;376:2319–28.
10. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. Arch Public Health. 2014;72:39.
11. Wallace BC, Dahabreh I, Schmid CH, Lau J, Trikalinos TA. Modernizing the systematic review process to inform comparative effectiveness: tools and methods. J Comp Eff Res. 2013;2:273–82.

12. La Manna A, Chisari A, Giacchi G, et al. Everolimus-eluting bioresorbable vascular scaffolds versus second generation drug-eluting stents for percutaneous treatment of chronic total coronary occlusions: technical and procedural outcomes from the GHOST-CTO registry. Catherter Cardiovasc Interv. 2016;88:155–63.

13. Ojeda S, Pan M, Romero M, et al. Outcomes and computed tomography scan follow-up of bioresorbable vascular scaffold for the percutaneous treatment of chronic total coronary artery occlusion. Am J Cardiol. 2015;115:1483–93.

14. Wiebe J, Liebetrut C, Dörr O, et al. Feasibility of everolimus eluting bioresorbable vascular scaffolds in patients with chronic total occlusion. Int J Cardiol. 2015;179:90–4.

15. Vaquerizo B, Barros A, Pujadas S, et al. One-year results of bioresorbable vascular scaffolds for coronary chronic total occlusions. Am J Cardiol. 2016;117:906–17.

16. Azpilin I, Giustino G, Ojeda S, et al. Procedural and Long-Term Outcomes of Bioresorbable Scaffolds Versus Drug-Eluting Stents in Chronic Total Occlusions: The BONITO Registry (Bioresorbable Scaffolds Versus Drug-Eluting Stents in Chronic Total Occlusions). Circ Cardiovasc Interv. 2016;9(10). https://doi.org/10.1161/CIRCINTERVENTIONS.116.004284.

17. Abellas-Sequeiros RA, Ocarranza-Sanchez R, Trillo-Nouche R, Gonzalez-Juanatey C, Gonzalez-Juanatey JR. Bioresorbable vascular scaffolds in coronary chronic total occlusions revascularization: safety assessment related to struts coverage and apposition in 6-month OCT follow-up. Heart Vessel. 2017. https://doi.org/10.1007/s00380-017-0980-9.

18. Mtomo S, Nagamura T, Fujino Y, et al. Bioresorbable Vascular Scaffolds for the Treatment of Chronic Total Occlusions: An International Multicenter Registry. Circ Cardiovasc Interv. 2017;10. https://doi.org/10.1161/CIRCINTERVENTIONS.116.004265.

19. Yaman AH, Yildiz A, Nasifov M, Tagtan A, Bashirov N, Gökçekin Ö. Clinical and angiographic outcomes at more than 1 year after treatment of chronic total occlusions with the everolimus-eluting bioresorbable vascular scaffold. Turk Kardiyol Dern Ars. 2016;44:647–55.

20. Kugler C, Markovic S, Rottbauer W, Wöhrl J. Bioresorbable scaffolds compared with everolimus-eluting stents for the treatment of chronic total coronary occlusion: clinical and angiographic results of a matched paired comparison. Coron Artery Dis. 2017;28:120–5.

21. Lesikar M, Lanocha M, Araszkiewicz A, et al. Percutaneous coronary intervention for chronic total occlusion of the coronary artery with the implantation of bioresorbable everolimus-eluting scaffolds. Poznan CTO-Absorb Pilot Registry. EuroIntervention. 2016;12:e144–51.

22. Özçel E, Tagtan A, Öztürk A, Özcan EE, Kilicarslan B, Özdoğan Ö. Procedural and one-year clinical outcomes of bioresorbable vascular scaffolds for the treatment of chronic total occlusions: a single-Centre experience. Cardiovascular J Afr. 2016;27:345–9.

23. Gökçekin O, Yaman AH, Latib A, et al. Evaluation of the safety of Everolimus-eluting Bioresorbable vascular scaffold (BVS) implantation in patients with chronic total coronary occlusions: acute procedural and short-term clinical results. J Invasive Cardiol. 2015;27:461–6.

24. Fam JM, Ojeda S, Garbo R, et al. Everolimus-eluting bioresorbable vascular scaffolds for treatment of complex chronic total occlusions. EuroIntervention. 2017;13:335–63.

25. Saad M, Abdin A, Thiele H, et al. Bioresorbable vascular scaffolds in a real-world patient population-results from a mid-term angiographic follow-up. J Interv Cardiol. 2016;29:341–7.

26. Polimeni A, Anadol R, Munzel T, Indolfi C, De Rosa S, Gori T. Long-term outcome of bioresorbable vascular scaffolds for the treatment of coronary artery disease: a meta-analysis of RCTs. BMC Cardiovasc Disord. 2017;17:147.

27. Sorrentino S, Giustino G, Mehran R, et al. Everolimus-eluting bioresorbable scaffolds versus Everolimus-eluting metallic stents. J Am Coll Cardiol. 2017;69:3055–66.

28. Stone GW, Gao R, Kimura T, et al. 1-year outcomes with the Absorb bioresorbable scaffold in patients with coronary artery disease: a patient-level, pooled meta-analysis. Lancet. 2016;387:1277–89.

29. Yang SS, Tang L, Ge GG, et al. Efficacy of drug-eluting stent for chronic total coronary occlusions at different follow-up durations: a systematic review and meta-analysis. Eur Rev Med Pharmacol Sci. 2015;19:1101–16.

30. Colmenarez HJ, Escaned J, Fernández C, et al. Efficacy and safety of drug-eluting stents in chronic total coronary occlusion revascularization: a systematic review and meta-analysis. J Am Coll Cardiol. 2010;55:1854–66.

31. Brugaletta S, Gomez-Lara J, Caballero J, et al. Ticagrelor versus clopidogrel for recovery of vascular function immediately after successful chronic coronary total occlusion revascularization: a randomized clinical trial. Am Heart J. 2018;204:205–9.

32. Polimeni A, Weissner M, Schockow K, et al. Incidence, clinical presentation, and predictors of clinical restenosis in coronary Bioresorbable scaffolds. JACC Cardiovasc Interv. 2017;10:1819–27.

33. Polimeni A, De Rosa S, Sabatino J, Sorrentino S, Indolfi C. Impact of intracoronary adenosine administration during primary PCI: a meta-analysis. Int J Cardiol. 2016;203:1032–41.

34. De Rosa S, Polimeni A, Petracco R, Davies JE, Indolfi C. Diagnostic performance of the instantaneous wave-free ratio: comparison with fractional flow reserve. Circ Cardiovasc Interv. 2018;11:e004613.

35. De Rosa S, Sievert H, Sabatino J, Polimeni A, Sorrentino S, Indolfi C. Percutaneous closure versus medical treatment in stroke patients with patent foramen ovale: a systematic review and meta-analysis. Ann Intern Med. 2018. https://doi.org/10.7326/M17-3033.

36. Anadol R, Lorenz L, Weissner M, et al. Characteristics and outcome of patients with complex coronary lesions treated with bioresorbable scaffolds Three years follow-up in a cohort of consecutive patients. Eurointervention. 2017. https://doi.org/10.4244/EIJ-D-17-00410.

37. Anadol R, Schnitzler K, Lorenz L, et al. Three-years outcomes of diabetic patients treated with coronary bioresorbable scaffolds. BMC Cardiovasc Disord. 2018;18:92.

38. Anadol R, Dimitriadis Z, Polimeni A, et al. Bioresorbable everolimus-eluting vascular scaffold for patients presenting with non ST-elevation-acute coronary syndrome: a three-years follow-up. Clin Hemorheol Microcirc. 2018;69:3–8.

39. Gori T, Weissner M, Gönner S, et al. Characteristics, predictors, and mechanisms of thrombosis in coronary Bioresorbable scaffolds: differences between early and late events. JACC Cardiovasc Interv. 2017;10:2363–71.

40. Biscaglia S, Ugo F, Ielasi A, Secco GG, Durante A, D’Ascenzo F, et al. Bioresorbable scaffold vs. second generation drug eluting stent in long coronary lesions requiring overlap: a propensity-matched comparison (the UNDERDOGS study). Int J Cardiol. 2016;208:40–7.

41. Gori T, Polimeni A, Adriaenssen T, et al. Predictors of stent thrombosis and their implications for clinical practice. Nat Rev Cardiol. 2018;15. https://doi.org/10.1038/s41569-018-0118-5.