Decision Analytic Markov Model Weighting Expected Benefits and Current Limitations of First-Generation Bioresorbable Vascular Scaffolds

Implications for Manufacturers and Next Device Iterations

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Background—Relative benefits of bioresorbable vascular scaffolds (BVS) compared with everolimus-eluting stents (EES) are expected to accrue after complete bioresorption.

Methods and Results—We built a decision analytic Markov model comparing BVS and EES for a contemporary percutaneous coronary intervention population. Procedure-related morbidity and outcome data from the available literature were used to derive model probabilities. The net benefit of BVS and EES was estimated in terms of quality-adjusted life expectancy. Under the assumption of no risk for device thrombosis and target lesion revascularization with BVS beyond 3 years, the equipoise in quality-adjusted life expectancy (12.86) between BVS and EES was achieved 19 years after implantation. The maximum tolerable excess risk of 3-year BVS thrombosis equalizing the model-predicted quality-adjusted life expectancy of BVS and EES at 10 years was 1.40, corresponding to an absolute tolerable rate of 1.45%.

Conclusions—At the currently observed relative increase in device thrombosis and under the extreme hypothesis of no scaffold thrombosis and target lesion revascularization beyond 3 years, the incremental benefit of BVS over EES becomes apparent only after 19 years. This simulation suggests that there is a small degree of benefit that clinicians and decision-makers may expect from the first-generation BVS at the current risk of device thrombosis. Manufacturers should target scaffold thrombosis rates <1.45% at 3 years to make their technologies attractive during a 10-year horizon. **(*Circ Cardiovasc Interv*. 2018;11:e005768. DOI: 10.1161/CIRCINTERVENTIONS.117.005768.)**

Key Words: bioresorbable vascular scaffolds ■ drug-eluting stents ■ life expectancy ■ risk ■ thrombosis

Bioresorbable scaffolds have been introduced in the market as a novel paradigm in the treatment of coronary artery disease by percutaneous coronary intervention (PCI). The goal of bioresorbable scaffolds is providing transient vessel support to prevent acute closure and recoil, eluting a drug to counteract neointimal proliferation, and finally resorbing completely to address substantial causes of long-term PCI failure with metallic stents, namely stent thrombosis and target lesion revascularization (TLR).[1]

See Editorial by Lafont and Mennuni

In the ABSORB III trial (A Clinical Evaluation of Absorb™ BVS, the Everolimus Eluting Bioresorbable Vascular Scaffold in the Treatment of Subjects With de Novo Native Coronary Artery Lesions), the first-generation Absorb bioresorbable vascular scaffold (BVS Abbott Vascular, Santa Clara, CA) was found noninferior to the everolimus-eluting stent (EES) with respect to target lesion failure at 1 year.[2] An interim analysis of the AIDA trial (Amsterdam Investigator-Initiated Absorb Strategy All-Comers) showed no significant difference between BVS and EES in the estimate of target-vessel failure at 2 years, but there was a significantly higher incidence of device thrombosis and target-vessel myocardial infarction (MI) in the BVS arm.[3] A meta-analysis of 4 randomized trials with individual patient data recently suggested that BVS is associated with increased rates of target lesion failure and device thrombosis cumulatively at 3 years and between 1 and 3 years compared with EES.[4] On September 2017, the manufacturer stopped the production of the first-generation ABSORB BVS because of low sales volumes, announcing enduring efforts in the clinical development of the second-generation BVS iteration.

Clearly, the first-generation BVS was associated with higher rates of device thrombosis compared with their metallic counterpart, not only during the first year after PCI but also beyond.[5–9] A BVS-specific implantation strategy called P-S-P (predilation, sizing, postdilation) has been introduced in the attempt to mitigate the occurrence of device thrombosis, but the notion of this risk persisting beyond 1 year

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WHAT IS KNOWN

- First-generation bioresorbable vascular scaffolds increased the risk of device thrombosis and target lesion failure compared with everolimus-eluting stents.
- The true benefit of bioresorbable vascular scaffolds is expected after their complete bioresorption.

WHAT THE STUDY ADDS

- Based on the available literature, we observed that the incremental benefit of bioresorbable vascular scaffolds over everolimus-eluting stents becomes apparent only after 19 years, when taking into consideration the currently observed relative increase in device thrombosis, as well as the hypothesis of no scaffold thrombosis or target-vessel revascularization after 3 years.
- With the production of the first-generation bioresorbable vascular scaffold now on hold, device refinements translating into better 3-year outcomes are key to ameliorate the risk–benefit balance of bioresorbable vascular scaffolds therapy.

suggests other nonprocedural factors (ie, late intraluminal scaffold dismantling and neoatherosclerosis) to also play a triggering role.[10] As such, it may be hypothesized that the true theoretical benefit of BVS cannot become apparent until the device disappears completely, which according to the manufacturer is expected to occur at ≈3 years from implantation. However, there is limited information available on the comparative efficacy of BVS and EES after 3 years, which makes it difficult to weigh and compare the consequences of events occurring while the BVS is in place (ie, device thrombosis) and the expected benefits during a lifetime horizon (ie, eradication of device thrombosis and TLR). On this background, we designed a decision analytic model to investigate the temporal interval that offsets the increased risk of 3-year device thrombosis with BVS as compared with EES, based on the theoretical assumption of no further events after complete bioresorption. In addition, we explored the sensitivity of multiple alternative scenarios that may be informative to patients with BVS implanted, as well as physicians, manufacturers and stakeholders, including the putative effect in the lifetime risk–benefit for 1) device bioresorption at a later-than-anticipated time point (ie, 5 instead of 3 years); 2) better implantation techniques and device ameliorations halving the initial relative increase of BVS in adverse cardiovascular events. Finally, we investigated the 3-year safety benchmark that justifies the implant of bioresorbable scaffolds in the current PCI landscape.

Methods

Study Design

We designed a Markov decision analytic model to forecast the clinical outcomes of BVS compared with EES during a time horizon of 25 years. A Markov model is a stochastic simulation of possible transitions among different clinical outcomes occurring in a cohort of patients after a definite treatment strategy.[11] The data, analytic methods, and study materials have been largely made available to other researchers in this article and the Appendix in the Data Supplement for purposes of reproducing the results or replicating the procedure.

Patient Population

The model was intended for a typical patient with coronary artery disease undergoing elective PCI, amenable to either treatment with BVS or EES and with no intraprocedural mortality.

Outcomes of Interest

Clinical events of interest were all-cause death (either cardiac or noncardiac), MI (either related or not related to the target lesion), revascularization (either related or not related to the target lesion), and definite or probable device thrombosis. In keeping with the Academic Research Consortium,[12] the events were defined as early when occurring within the first 30 days after implantation, late between 30 days and 1 year, and very late beyond 1 year.

Decision Model Structure

A Markov model was constructed covering all possible outcomes of interest for a PCI patient after the index procedure. We analyzed cycles of 1-year length built by a consecutive series of nodes typically encompassing 2 mutually exclusive alternatives (sequential 2-level chance nodes). The following health states were considered: (1) survival without adverse events, (2) survival after MI, and (3) all-cause death.

Figure 1 depicts the initial treatment (BVS versus EES) and the potential 1-year outcomes in the form of a decision tree. During the initial cycle, based on the assumption of no procedural mortality, patients could experience noncardiac death or cardiac death unrelated to PCI. In the absence of death, patients were at risk for early device thrombosis. All patients with early device thrombosis were assumed to either die or experience a nonfatal target lesion MI. For simplicity, all patients with nonfatal thrombosis or MI were assumed to undergo TLR and were at risk for procedure-related mortality. Patients were not considered at risk for restenosis within the first month, consistent with known biology. Patients alive were assumed to be at risk for subsequent late thrombosis and revascularization ≤1 year. Patients undergoing revascularization were assumed to present with either MI or no MI. Options for revascularization included PCI or coronary artery bypass grafting. Background risks of noncardiac death and cardiac death were accounted in the model.

Beyond 1 year and ≤3 years, survivors with either BVS or EES were at risk of device thrombosis and repeat revascularization in addition to background risks of noncardiac death, cardiac death, and MI. Patients who experienced device thrombosis could either die or experience a nonfatal MI. Again, all surviving patients with nonfatal device thrombosis or MI were assumed to undergo revascularization and were at risk for procedure-related mortality. Beyond 3 years, the relative risk of device thrombosis and TLR with BVS compared with EES was set to zero, consistent with the primary study hypothesis. Tracker variables were used in the model to keep a record of all the events experienced by simulated patients.

Data Sources

To inform the Markov model, absolute and relative probabilities of procedural success, complications, and outcomes after PCI were obtained by a systematic review of published medical reports (Table 1; Table I in the Data Supplement).[11,13–27] To more accurately reflect a contemporary real-world PCI scenario, whenever possible, absolute event rates were calculated with the contribution of registry data reflecting broader populations than those included in randomized clinical trials (Table II and Figures I through III in the Data Supplement).

The relative risks of device thrombosis and TLR (for BVS versus EES) were obtained from updated corresponding meta-analyses of randomized clinical trials (Table 2; Appendix in the Data Supplement;

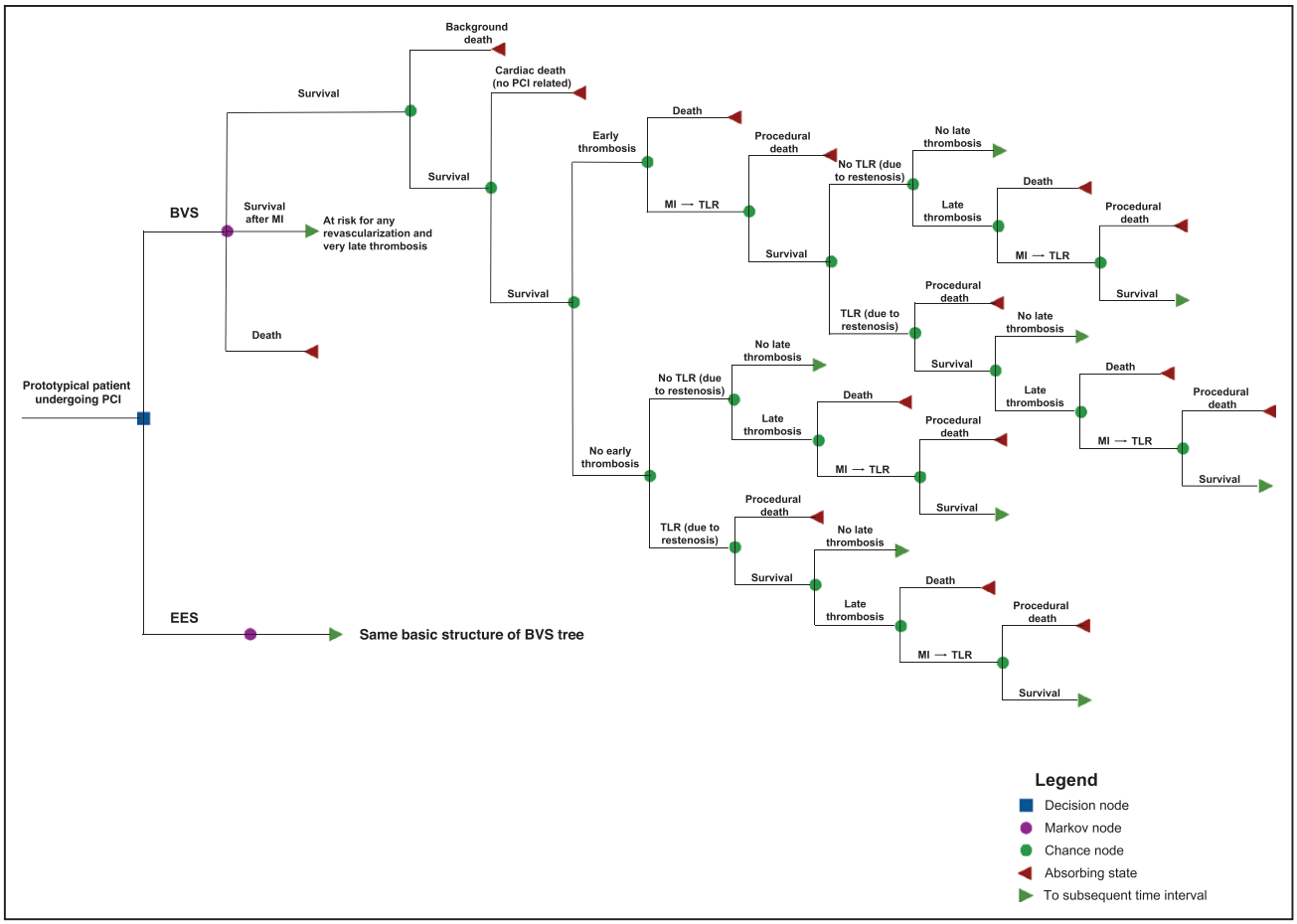

Figure 1. Schematic of the Markov model. **A**, Simplified decision tree representing the possible outcomes of bioresorbable vascular scaffold (BVS) and everolimus-eluting stent (EES) in the first 30 days and 1 year after the index procedure. **B**, State transition diagram showing the initial therapeutic decision between BVS and EES and possible outcomes after the first year of life after the index procedure. MI indicates myocardial infarction; PCI, percutaneous coronary intervention; and TLR, target lesion failure.

Figures IV through VIII in the Data Supplement). The TROFI II trial was excluded from these meta-analyses because it only enrolled patients with ST-segment–elevation MI.[28]

Quality-of-Life Adjustment

The outcomes of BVS and EES were evaluated in terms of quality-adjusted life-years (QALY). In this context, 1 year without thrombosis, revascularization, or death was assumed as a year of perfect health (QALY=1), whereas death was regarded as QALY=0. For repeat revascularization procedures, a temporary disutility of 0.06 was applied to the relevant cycle.[29] In addition, we considered an incremental disutility of 0.08 for revascularization with coronary artery bypass grafting over PCI to account for higher invasiveness of the procedure and prolonged in-hospital stay.[30] In patients experiencing MI, QALY were penalized in the long term, consistently with the notion that health-related quality of life is impaired with respect to the general population also several years after MI, in particular, among younger patients.[31] QALY adjustments for health states included in the model are summarized in Table 3.[29,30,32]

Statistical Analysis

The design of the model and all analyses were conducted using TreeAge Pro 2015 (TreeAge Software, Inc, Williamstown, MA). Quality-adjusted life expectancy (QALE) was calculated for each treatment. We considered the strategy with the highest QALE to be preferred during the study time horizon. A Monte Carlo simulation was performed by microsimulation trials to estimate the absolute number of events for each treatment strategy. The predicted number of events was compared between BVS and EES using $\chi 2$ or Fisher exact tests, as appropriate. Absolute risk reductions and numbers needed to treat were calculated.

Impact of Absorption Time, Implantation Technique, and Device Ameliorations

We investigated the impact on outcomes of an alternative simulated scenario where complete BVS resorption occurs at 5 years. In the absence of comparative data on very late thrombosis and TLR risk beyond 3 years for BVS and EES, we assumed the relative risk between 3 and 5 years to constantly replicate that observed between 1 and 3 years. The potential impact of an optimized implantation strategy or future device amelioration was also investigated based on the hypothesis that the relative risk of early, late, and very late thrombosis for BVS versus EES is at least halved if a BVS has been optimally implanted or a better scaffold device enters the market. Finally, we investigated the safety margin (ie, risk of device thrombosis at 3 years) for which the difference in QALE between BVS and EES equalizes within 10 years.

Sensitivity Analyses

Because our model was based on several assumptions, we performed 1-way and probabilistic sensitivity analyses to identify whether variations in these assumptions may have a substantial affect on the study findings. Model inputs were based on their 95% confidence interval (where available) or arbitrarily defined. Probability distributions and the range of variation for different parameters tested in sensitivity analyses are shown in Table III in the Data Supplement. We

Table 1. Probability Estimates Used in the Decision Analytic Model

Variable	Estimate		Source
	EES	BVS	
Thrombosis, %			Pooled analysis (Appendix in the Data Supplement)
Early (0–30 d)	0.39	0.76	
Late (>30 d to 1 y)	0.19	0.59	
Very late (>1 y)	0.08, y^{-1}	0.39, y^{-1}	
TLR, %			Pooled analysis (Appendix in the Data Supplement)
Late (>30 d to 1 y)	2.81	3.09	
Very late (>1 y)	0.88, y^{-1}	1.22, y^{-1}	
Common estimates between EES and BVS, %			
Cardiac mortality (not related to PCI)	1.84, y^{-1}		Lee at al[13] and Aggarwal et al[14]
TLR presenting as ACS	34		Hayes et al[15]
Non-target vessel–related MI	0.68, y^{-1}		Chacko et al[16]
Management of nonfatal MI, %			
PCI	94.5		Gu et al[17]
CABG	5.5		Gu et al[17]
Management strategy for TLR, %			
PCI	87.9		Loponen et al[18]
CABG	12.1		Loponen et al[18]
Management strategy for thrombosis, %			
PCI	92		Hwang et al[19]
CABG	8		Hwang et al[19]
Mortality after thrombosis, %			
Early	20		Garg et al[11]
Late	20		Garg et al[11]
Very late	10.5		Kimura et al[20]
Procedural mortality, %			
PCI (elective)	0.18		Valle et al[21]
CABG (elective)	2.66		Peterson et al[22]
PCI (emergent)	2.26		Brennan et al[23]
CABG (emergent)	2.91		Voisine et al[24]
Post procedure/event mortality, %			
CABG	6.2		Wu et al[25]
PCI	2.78		Iqbal et al[26]
Nonfatal MI	16.7, y^{-1}		Shah et al[27]

ACS indicates acute coronary syndrome; BVS, bioresorbable vascular scaffold; CABG, coronary artery bypass grafting; EES, everolimus-eluting stents; MI, myocardial infarction; PCI, percutaneous coronary intervention; and TLR, target lesion revascularization.

graphically displayed the results of 1-way sensitivity analyses in the form of an incremental tornado diagram. This approach is useful to assess the influence of model parameters on the estimate of the incremental QALE calculated between 2 strategies. The probabilistic sensitivity analysis was performed to assess the impact of joint uncertainty in each of the modeling parameters on the distribution of the expected QALE difference between BVS and EES.

Table 2. Relative Risk Estimates for Bioresorbable Vascular Scaffolds Versus Everolimus-Eluting Stents

Variable	RR Estimate	95% CI	*P* Value	Source
Thrombosis				
Early (0–30 d)	1.95	1.30–2.93	0.01	Pooled analysis*
Late (>30 d to 1 y)	3.12	0.38–25.65	0.18	Pooled analysis*
Very late (1–3 y)	4.91	3.70–6.51	<0.01	Pooled analysis*
Very late (>3 y)	0	…	…	Study assumption
TLR				
Late (>30 d to 1 y)	1.10	0.82–1.47	0.45	Pooled analysis*
Very late (1–3 y)	1.39	1.05–1.83	0.03	Pooled analysis*
Very late (>3 y)	0	…	…	Study assumption

CI indicates confidence interval; RR, relative risk; and TLR, target lesion revascularization.

*See Appendix in the Data Supplement for full details.

Results

Patient Population

A total of 65 studies reporting outcomes from 57 231 patients were selected for the pooled analysis of absolute risk probabilities (Table I in the Data Supplement). Clinical characteristics of these patients are shown in Table IV in the Data Supplement. Overall, the mean age was 63 years, and 75% of patients were men. The prevalence of diabetes mellitus and presentation with an acute coronary syndrome were 31% and 43%, respectively. Diabetes mellitus (26% versus 35%; *P* for interaction, 0.014) was less frequent in combined randomized and observational studies of BVS compared with EES. However, no difference in clinical characteristics between EES and BVS was observed in the pooled analysis of the 6 randomized studies used to compute relative risk probabilities.

Model Calibration and Predicted Number of Events

The model was well calibrated with predicted rates of all-cause mortality at 5 years of 11.0% and 10.7% for BVS and EES,

Table 3. Quality-of-Life Adjustments and Disutility

Variable	QALY Correction	Source
Year without event	1	…
Year with CAD and no revascularization	0.85	Cohen et al[29]
Year with CAD after MI	0.70	Sullivan et al[32]
Disutility for revascularization (temporary)	0.06	Cohen et al[29]
Incremental disutility of CABG vs PCI (temporary)	0.08	Cohen et al[30]

CABG indicates coronary artery bypass grafting; CAD, coronary artery disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; and QALY, quality-adjusted life year.

Table 4. Model-Predicted Number of Events (10 000 Patients per Group)

Event	BVS	EES	Absolute Difference
All-cause mortality	4360	4394	34
Early thrombosis	79	47	32
Death after early thrombosis	16	6	10
Late thrombosis	56	19	37
Late TLR (excluding thrombosis or ACS presentation)	291	262	29
Very late thrombosis	110	123	13
Very late TLR	324	1407	1083

ACS indicates acute coronary syndrome; BVS, bioresorbable vascular scaffolds; EES, everolimus-eluting stents; and TLR, target lesion revascularization.

respectively, consistently with contemporary long-term outcomes of second-generation drug-eluting stents.[33] Predicted number of events during a 25-year time horizon based on Monte Carlo microsimulation (10 000 patients for each group) is shown in Table 4. In line with the model design, there was an increase in the rate of model-predicted early (0.8% versus 0.5%) and late (0.6% versus 0.2%) thrombosis of BVS compared with EES. Conversely, the rate of very late TLR was significantly reduced with BVS (3.2% versus 14.1%). Predicted rates of very late events at 5, 10, 15, and 20 years are shown in Table V in the Data Supplement. The predicted rate of device thrombosis was numerically higher in the EES group at 20 years but not at 5, 10, and 15 years. The predicted rate of very late TLR was reduced with BVS at 10, 15, and 20 years. The mortality rate was substantially similar at all time points.

QALE of BVS and EES Strategies

Under the assumption of no risk for device thrombosis and TLR beyond 3 years with BVS, the model-predicted QALEs for a prototypical patient undergoing PCI were 15.789 and 15.758 for BVS and EES, respectively (reflecting a small difference in QALYs of 0.031 favoring BVS). However, EES represented the preferred strategy for almost 2 decades after PCI. In fact, the equipoise in QALE between the 2 strategies (12.86) was achieved 19 years after implantation (Figure 2). Based on the alternative hypothesis of complete BVS resorption occurring at 5 years from implant, the equipoise in QALE between the 2 strategies (17.060 QALYs) was observed after 28 years. Conversely, assuming a halved relative risk of early, late, and very late BVS thrombosis because of better implantation strategies or improved device characteristics, the equalization in QALE between BVS and EES (8.101 QALYs) occurred at 11 years from implant. At the currently observed relative risks of late and very late TLR (Table 2), the maximum tolerable excess risk of 3-year BVS thrombosis equalizing the model-predicted QALEs of BVS and EES at 10 years was 1.40 (Figure 3), corresponding to an absolute estimated rate of 1.45%.

Sensitivity Analyses

The results of 1-way sensitivity analyses, testing for the impact of key parameters on model performance, identified cardiac mortality not related to PCI and noncardiac mortality as influential parameters. Conversely, the model was insensitive to reasonable variations in most other model parameters (Appendix in the Data Supplement; Figure IX in the Data Supplement). Sensitivity analyses for the incremental QALE estimate between BVS and EES are shown in Figure 4. Not surprisingly, relative risk variations in device thrombosis and TLR influenced the predicted difference between BVS and EES. In addition, mortality after thrombosis within the first year and the rate of very late TLR were found to be potentially influential. However, the results of the probabilistic sensitivity analysis were consistent with the main analysis, confirming the small net gain in QALE with BVS during the time horizon of the study (Δ=0.024).

Discussion

Abating the risk of very late stent failure with a coronary bioresorbable device is intuitively appealing.[34] However, the anticipated benefit of a novel technology should not come at the price of excess risk in the initial period. To preserve adequate early and midterm support of the vessel, BVS require

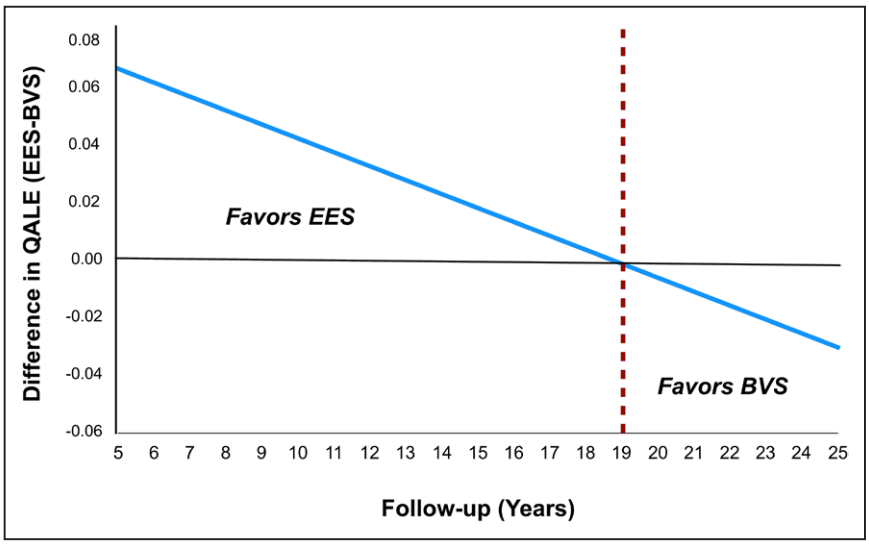

Figure 2. Difference in quality-adjusted life expectancy (QALE) between bioresorbable vascular scaffold (BVS) and everolimus-eluting stent (EES) over time. The difference in QALE favors EES ≤19 years, whereas BVS become a preferable strategy beyond 19 years.

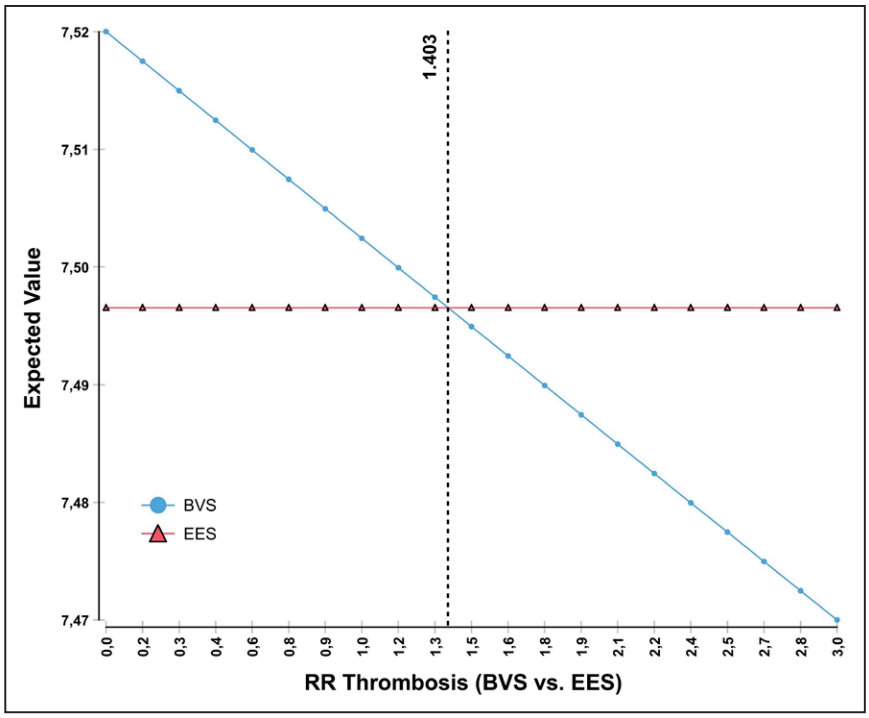

Figure 3. Maximum tolerable excess risk of thrombosis equalizing the quality-adjusted life expectancy (QALE) of bioresorbable vascular scaffolds (BVS) compared with everolimus-eluting stents (EES) within 10 years. At the currently observed relative risks (RRs) of late and very late target lesion failure, the maximum tolerable excess risk of 3-year BVS thrombosis equalizing the model-predicted QALEs of BVS and EES was 1.40, corresponding to an absolute estimated rate of 1.45%.

their dissolving struts to be thicker and wider than those of contemporary drug-eluting stents.[1] However, increased strut thickness and width have been associated with more thrombogenicity in animal models;[35] this may contribute to explain the increased thrombogenicity of BVS in comparison with EES.[5,7–9] To inform our decision model, we conducted updated meta-analyses and found that the risk of device thrombosis was ≈2-fold increased at 30 days, 3-fold increased at 1 year and almost 5-fold increased after 1 year with BVS compared with EES. One may advocate that even small excesses in scaffold thrombosis while the device is in place can be accepted in view of later benefits in reducing thrombosis and the need for revascularization when the device disappears at ≈3 years. Given the absence of very long-term comparative data (a knowledge gap, which will remain for many years ahead), we used a Markov decision analytic model to quantify the degree to which the current uncertainty in the risk of BVS failure would affect decision-making at the time of PCI. In particular, we sought to define (1) the temporal interval needed to offset the currently observed increased risk of 3-year thrombosis with BVS as compared with EES, and (2) what threshold of initial incremental risk at 3 years would outweigh the putative benefits of no BVS failure within 10 years from PCI.

We found that at the current risk of 3-year BVS thrombosis and under the assumption of no risk for very late events beyond 3 years, BVS represent a preferable strategy for an elective PCI patient during a long-lasting time horizon (ie, 25 years, corresponding to a lifetime horizon for a typical 60-year-old patient enrolled in ABSORB III or AIDA). However, under the hypothetical scenario of no thrombosis and TLR of BVS between 3 and 25 years, we found that the observed 3-year increase in device thrombosis would be offset only after 19 years from PCI. This estimation worsens ≤28 years in the alternative scenario where the BVS does not disappear before 5 years. These simulations suggest that there is a small degree of benefit that clinicians and decision-makers may expect from BVS to make this strategy attractive at the current risk of device thrombosis.

There is emerging evidence and belief that optimizing the implantation technique of BVS decreases the risk of device thrombosis.[36] Improvements of the current BVS iteration and introduction of thinner-strut bioresorbable scaffolds are in the pipeline, which may also be instrumental in decreasing this risk. Indeed, the polymer characteristics of first-generation BVS might be responsible of undesired phenomena that can be accounted for with improved manufacturing, including inflammatory reactions during degradation, impaired endothelialization because of the 160-μ strut thickness, breakage at implantation, and late intraluminal dismantling.[1] According to our model, halving the risk of device thrombosis by means of improved technique or improved scaffold design characteristics would result in QALE equalization at 11 years.

Combination of the long-term results of the ABSORB III and ABSORB IV trials, encompassing ≈5000 patients, has been planned to test the hypothesis that BVS is superior to EES with respect to target lesion failure in the landmark period between 3 and 7 to 10 years. We used our model to forecast which improvement in the relative risk of BVS thrombosis at 3 years compared with EES is necessary to make the trade-off between the initial hazard and long-term safety more favorable to BVS. We found that the risk of BVS thrombosis should be <1.40 (relative) or 1.45% (absolute) at 3 years. This threshold may serve as a useful reference for current and future studies investigating BVS and other bioresorbable scaffold technologies.

In aggregate, our study suggests that, despite the increased risk of early thrombosis, BVS may still provide

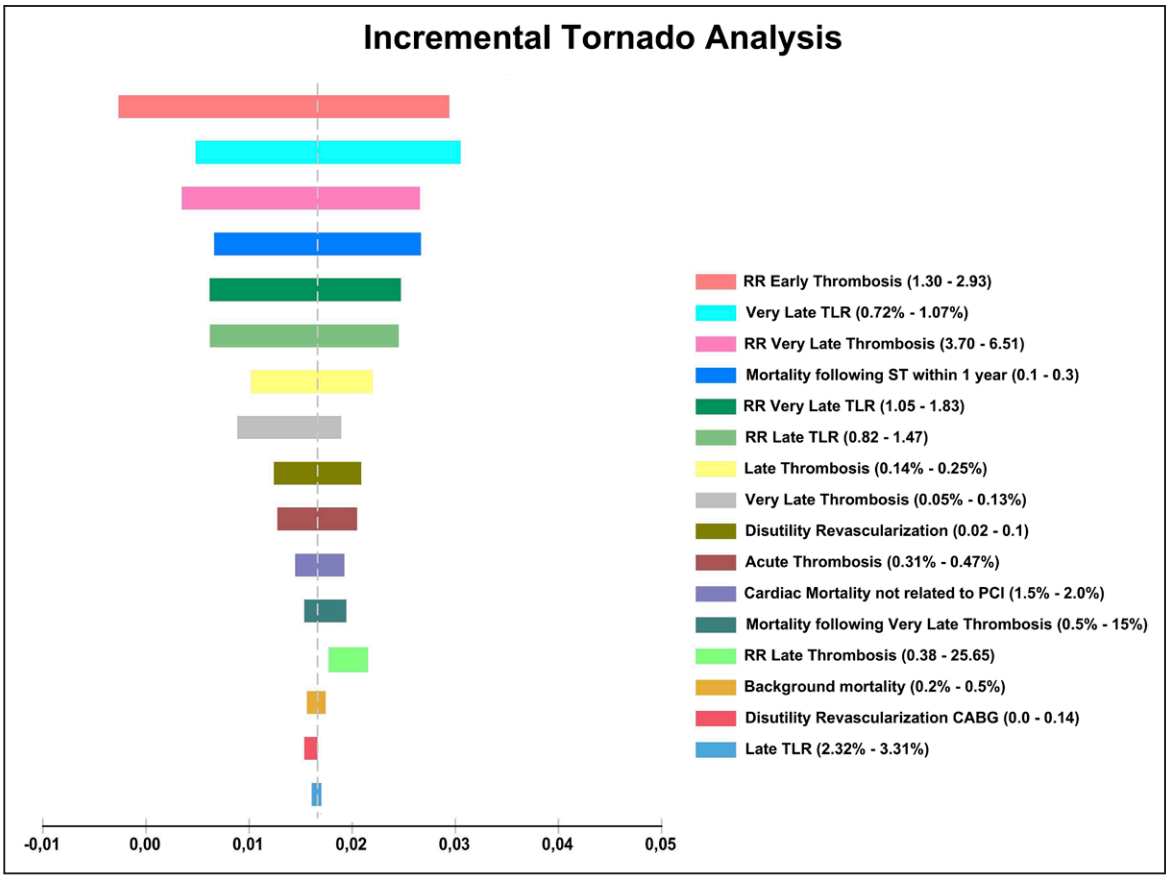

Figure 4. Sensitivity analyses (tornado diagram). One-way sensitivity analyses for incremental estimates of quality-adjusted life expectancy between bioresorbable vascular scaffold and everolimus-eluting stent. CABG indicates coronary artery bypass grafting; PCI, percutaneous coronary intervention; RR, relative risk; ST, stent or scaffold thrombosis; and TLR, target lesion failure.

a theoretical net clinical benefit to patients, but only if the expected risk of stent failure beyond 3 years with EES is substantial and the difference in favor of BVS is profound. As the benefit in reducing PCI failure decreases, the tolerable excess risk of 3-year thrombosis must also diminish to preserve the value of BVS as the best treatment option in a general PCI setting. With the production of the first-generation BVS now on hold, device refinements translating into better 3-year outcomes are key to ameliorate the risk–benefit balance of BVS therapy.

Study Limitations

As in any decision analysis, we were limited by reliance on the available data. Understandably, our findings were sensitive to reasonable variations in the relative risks of clinical events considered in the model, but the small gain in QALE remained consistent in a probabilistic sensitivity analysis taking into account a range of plausible possibilities rather than fixed estimates alone. Early thrombosis rates of BVS and EES were obtained from an updated large meta-analysis of patients from mostly observational studies, reflecting contemporary use of BVS across countries. Patients and lesions treated in BVS registries may be characterized by lower clinical anatomic complexity with respect to EES cohorts (ie, lower incidence of diabetes mellitus, selective use in more complex lesion types, and exclusion of large and small vessels). Indeed, the penetration of the BVS technology in daily clinical practice has been low even before marketing withdrawal. This aspect is unlikely to have represented a source bias in favor of BVS because the most reliable relative risk for the comparison of BVS and EES was obtained from the meta-analysis of 6 randomized trials, where no confounding applies. Another potential caveat is that relative risk estimates were assumed constant over time, despite the known stochastic and time-varying nature of risk in a real-world scenario. Finally, it should be noted that the results of this study are applicable to the comparison of EES with the first-generation ABSORB BVS, although an alternative scenario for novel scaffolds with a better safety profile has also been reported.

Conclusions

Based on a Markov decision analytic model incorporating the best available data in the literature, we found that at the currently observed relative increase in thrombosis at 3 years, benefits in QALE of BVS over EES become apparent only after 19 years. A 1.40 excess risk of BVS thrombosis while the device has not yet disappeared is the maximum tolerable gap that equalizes the QALEs of BVS and EES within 10 years.

Disclosures

Drs Capodanno and Tamburino have received speaker's fees and consulting honoraria from Abbott Vascular. The other authors report no conflicts.

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