Review

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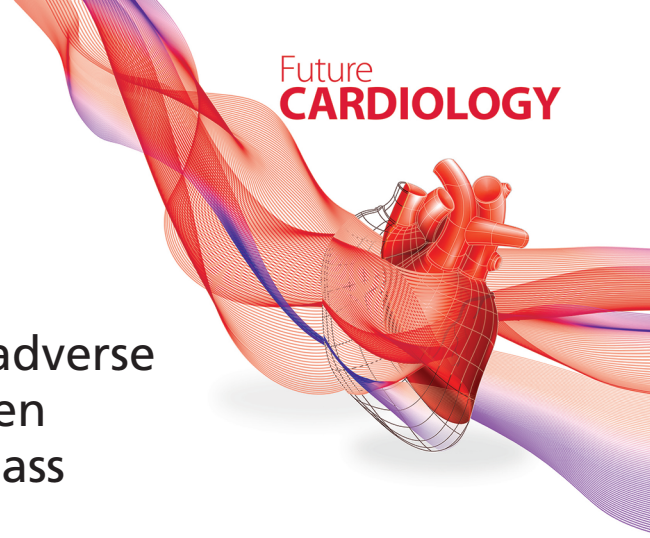

Increased incidence of serious late adverse events with drug-eluting stents when compared with coronary artery bypass surgery: a cause of concern

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Percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) in pre-drug-eluting stents (DESs) era, randomized trials and meta-analysis showed that the extension of coronary artery disease was not associated with a better survival with CABG, and only diabetic patients had an inferior survival with PCI. After the introduction of DES, we would expect a substantial improvement in PCI results compared with CABG, narrowing the gap between both revascularization strategies, However, on the contrary, most randomized studies between DES and CABG showed that rate of recurrences remained and there is an unexpected increased of late serious adverse events including spontaneous myocardial infarction and death. In this review, we try to described each of these problems and find out explanations for these new findings searching for potential solutions.

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Keywords: acute coronary syndromes • CABG • ischaenic heart disease • percutaneous coronary interventions • stents, Syntax Score, ERACI Score

It has been 55 and 42 years, since the first coronary artery bypass graft (CABG) [1,2] and coronary balloon angioplasty (POBA) were performed, respectively [3].

After that we have to wait more than two decades until first randomized clinical trials (RCTs) comparing CABG with POBA in multiple vessel disease (MVD) were reported [4].

After those years, multiple RCTs were performed between percutaneous coronary intervention (PCI), either with POBA or bare metal stents (BMS), versus CABG in patients who required myocardial revascularization. These studies persistently revealed a similar incidence of long-term events, including death and acute myocardial infarction (MI), despite having a greater number of target vessel revascularization (TVR) and having less complete revascularization (Figure 1 and Table 1) with the PCI [5,6].

In these trials, the extent of coronary artery disease (CAD) was not associated with a better survival with CABG, and only diabetic patients had an inferior survival with percutaneous procedures.

After the introduction of drug-eluting stents (DESs) in clinical practice, superiority of DES over BMS had been largely demonstrated either first-generation (DES-1) [12,13] or the latest (DES-2) [14] in head-to-head comparison in several RCTs and meta-analysis [14].

Therefore, we would expect a substantial improvement in PCI results compared with CABG, narrowing the gap between both revascularization strategies translating in few repeat revascularization procedures, target vessel revascularization (TVR) and incidence of TVR MI [14].

However, that was not the case and on the contrary, the great majority of RCTs between DES and CABG showed that the hiatus in the rate of recurrences remained and there is an unexpected increased rate of late serious adverse events beyond one year in most of them including spontaneous MI and death in patients treated with DES in both diabetic and nondiabetic population [7,15,16].

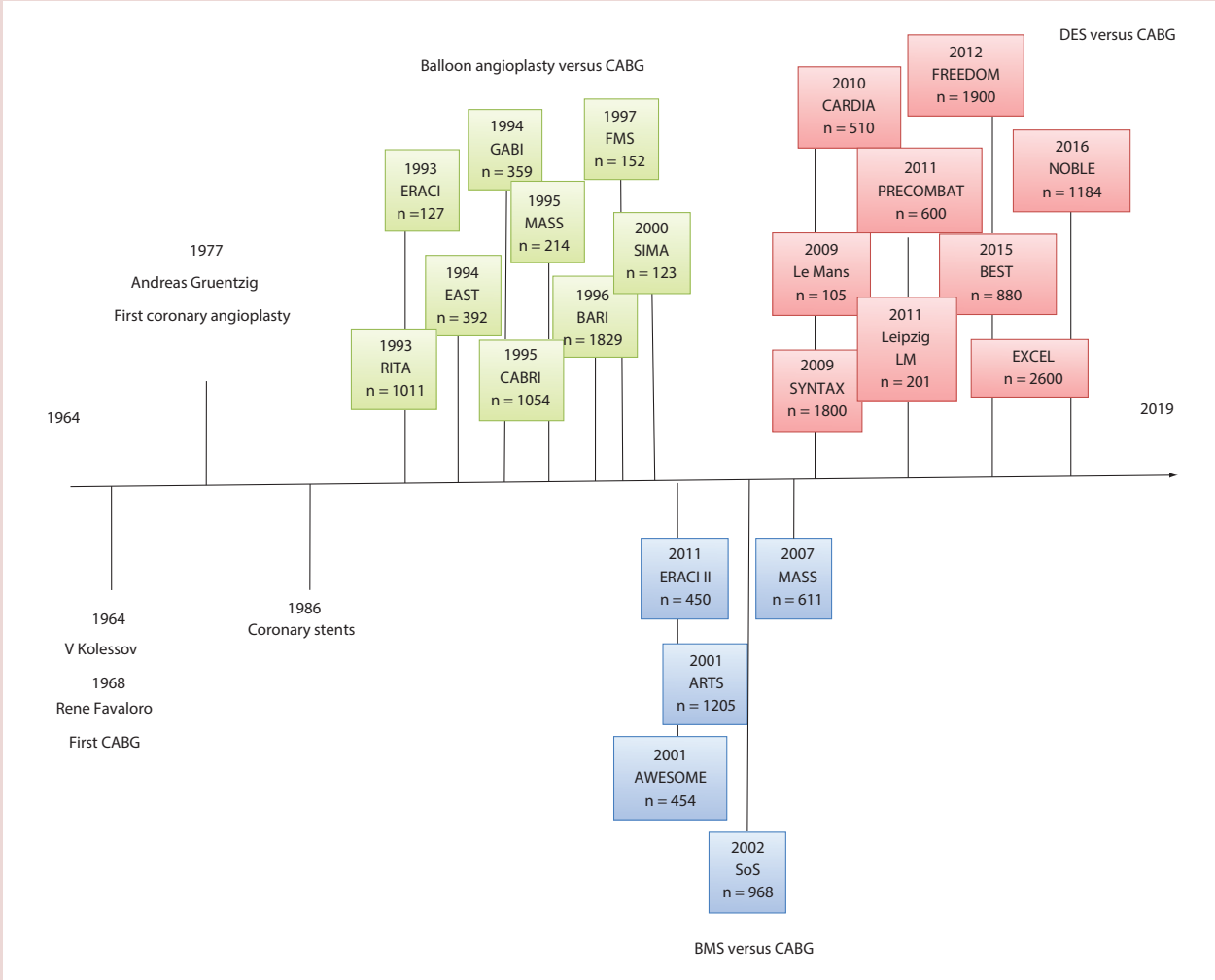

Figure 1. Randomized Controlled Trials of myocardial revascularization.
CABG: Coronary artery bypass graft; DES: Drug-eluting stent.
Data taken from [1–6].

One of the explanations for this phenomenon was that, DES-1 was associated with an undesirable rate of late and very stent thrombosis (ST) [17].

SYNTAX trial showed a ST incidence of 15.4% at 5 years of follow-up, which was linked to an increased incidence of death and MI [15].

When DES-2 was introduced in clinical practice, they significantly improved safety compared with DES-1, in terms of stent mal-apposition and stent struts coverage which was soon translated by a significant lower incidence of late and very late ST as well for the requirements of long-term dual antiplatelet therapy (DAPT) [18].

However, in spite of such improvement, when compared with CABG, DES-2 are still having greater incidence of late adverse serious cardiac events as reflected by the incidence of spontaneous MI seen in all DES-2 versus CABG trials as were reported in BEST, [8] NOBLE [9] and EXCEL [10] trials.

A pooled data from SYNTAX (DES-1) and BEST (DES-2), comparing CABG versus DES in a nondiabetic population with multiple vessel CAD, CABG was associated at 5 years with significantly lower incidence of death (DES 10% vs CABG 6.7%; $p = 0.037$), MI (DES 8.9% vs CABG 3.4%; $p < 0.001$) and death/MI and CVA (DES 17.6 vs 12.2% CABG; $p < 0.011$) Figure 2. These findings were seen across all groups without trial or stent

Table 1. Completeness of revascularization in randomized clinical trials.

Trials	CABG patients (n)	PCI patients (n)	CABG complete revascularization	PCI complete revascularization	p-value
EAST	194	198	99%	75%	0.002
ARTS	605	600	84.1%	70.5%	0.001
ERACI	64	63	88%	51%	0.001
CABRI	513	541	82%	59%	0.001
RITA	501	510	97%	81%	0.003
MASS II	203	205	74%	41%	0.001
SYNTAX	897	903	63%	57%	0.005
ERACI II	225	225	85%	50%	0.002
BEST	442	438	72%	51%	<0.001
NOBLE	564	592	95%	92%	0.53
EXCEL	957	948	n/a	n/a	n/a
PRECOMBAT	300	300	70.3%	68.3%	0.60

CABG: Coronary artery bypass graft; PCI: Percutaneous coronary intervention.
Data taken from [4,5,7–11].

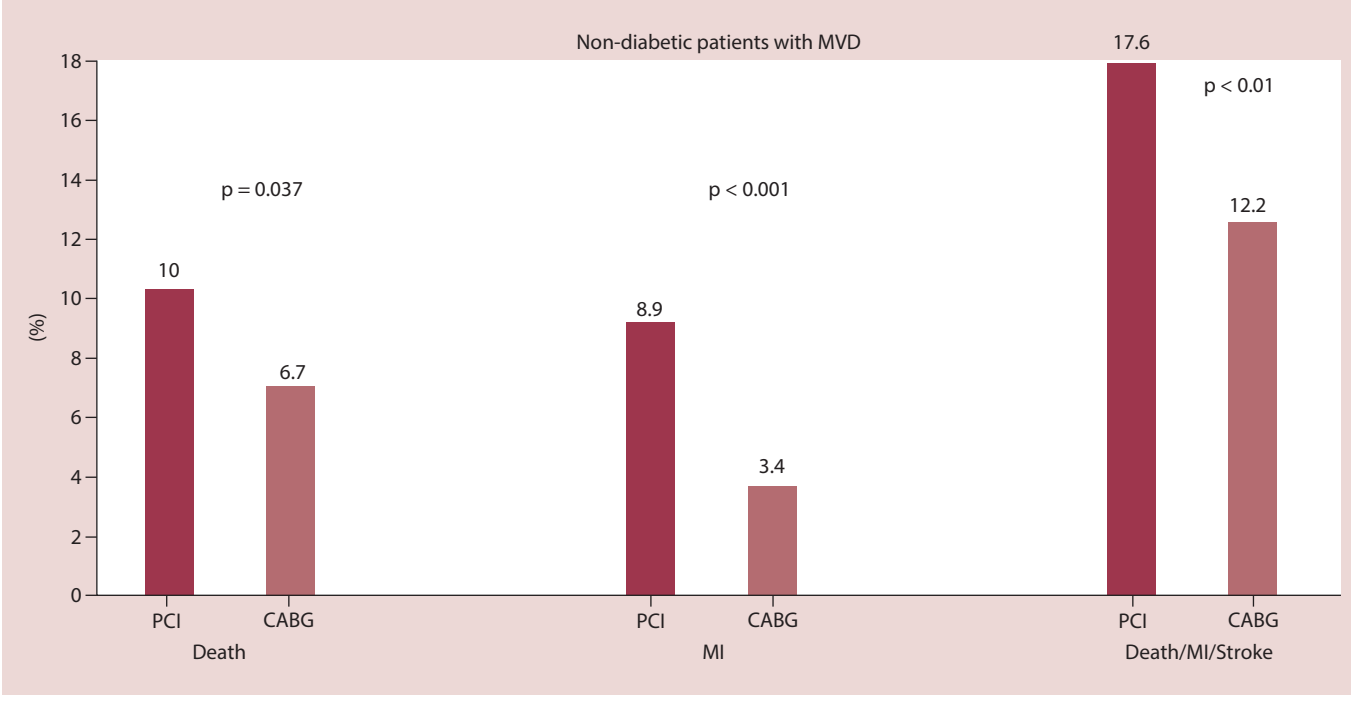

Figure 2. Pooled data from nondiabetic patients with multiple vessel disease included in Syntax and Best trials.
CABG: Coronary artery bypass graft, MI: Myocardial infarction; MVD: Multiple vessel disease; PCI: Percutaneous coronary intervention.
Data taken from [19].

interaction for the primary outcome. This observation for the first time suggested that CABG had safety advantages over PCI in nondiabetic population with MVCAD [19].

On contrary, if we remembered previous data of RCT with BMS versus CABG, in MVD in nondiabetic and diabetic population (ARTS, ERACI II, MASS and SoS), [20] in this meta-analysis from individual level patient data, they didn't find any differences between both revascularization strategies in either death (PCI 8.5% vs CABG 8.2% p = 0.78), MI (PCI 6.6% vs CABG 6.1% p = 0.68) or death/MI/CVA (PCI 14.2% and CABG 14.6 p = 0.78) without interaction between diabetics and nondiabetics (p = 0.65). Regardless differences in baseline characteristics (Table 2), if we perform an indirect analysis among FREEDOM, [16] SYNTAX [7] and BEST [8] versus this meta-analysis (ARTS, ERACI II, MASS II and SoS) [20] at 5 years of follow-up large differences in serious adverse events

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Table 2. Baseline characteristics among patients in FREEDOM, SYNTAX and BEST trials versus bare metal stent meta-analysis.

Characteristic	FREEDOM/SYNTAX/BEST trials (n = 1590)	Meta-analysis (n = 1518)	p-value
Age (years)	63.5	61.6	0.50
Hypertension	63.5%	50.5%	<0.01
Previous MI	26.5%	42.8%	<0.01
ACS	34.5%	28.5%	0.07
Euroscore	2.7%	n/a	n/a
Smoker	18.4%	28.3%	<0.01
Peripheral disease	5.8%	7%	0.22
Two-vessel disease	13.6%	59.3%	<0.01
Three-vessel disease	86.4%	36.1%	<0.01
Complete revascularization with PCI	54%	54%	0.98
Diabetic patients	59%	18%	<0.01
LMCA	0%	1%	1.00

ACS: Acute coronary syndrome; BMS: Bare metal stent; LMCA: Left main coronary artery stenosis; PCI: Percutaneous coronary intervention.
Data taken from [7,8,16,19,20].

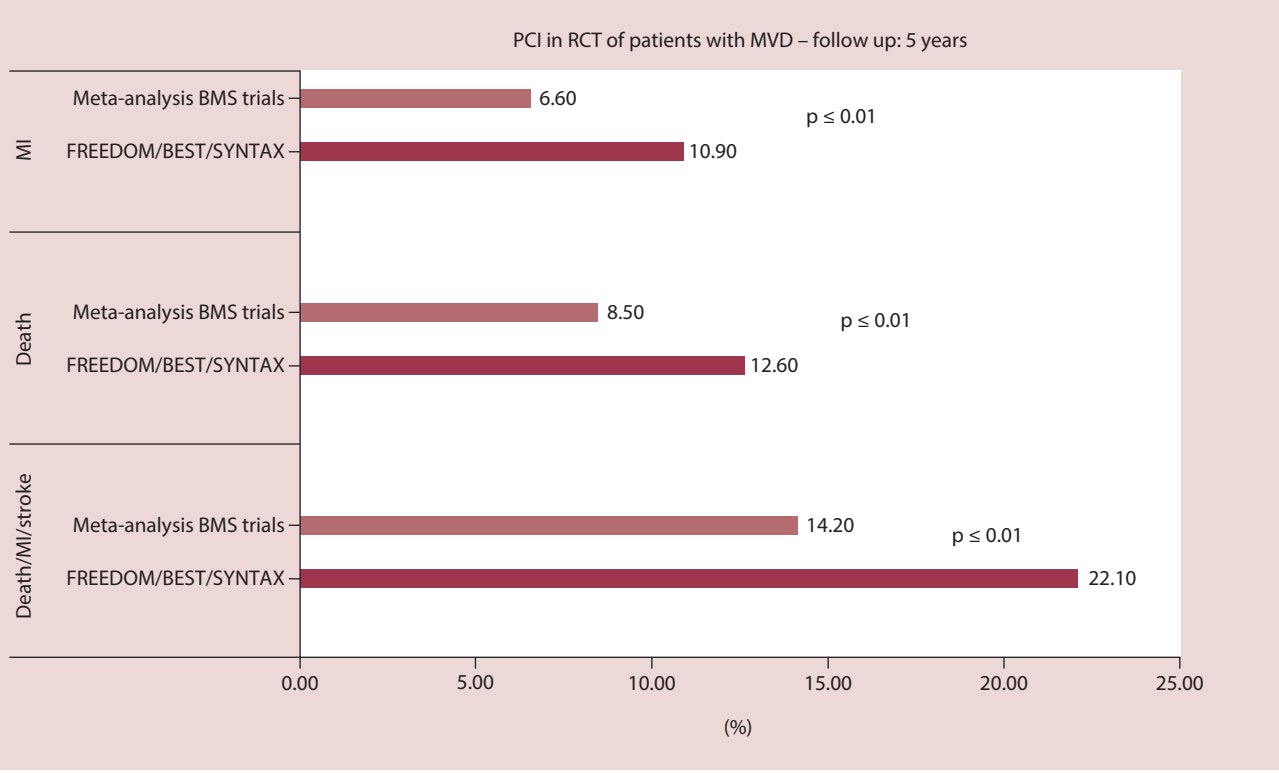

Figure 3. Percutaneous coronary intervention results at 5 years: cardiac adverse cardiac events from randomized controlled trials among patients treated with bare metal stents and drug-eluting stents.
Meta-analysis, FREEDOM, SYNTAX and BEST trials.
Event rate from a meta-analysis are related to crude events rate described in Table 2 of [20].
BMS: Bare metal stent; MI: Myocardial infarction; PCI: Percutaneous coronary intervention; RCT: Randomized clinical trial.
Data taken from [7,8,16,20].

were seen (death 8.5 vs 12.6% p = 0.001, MI 6.6 vs 10.9% p = 0.001 and death/MI/ cerebrovascular accident (CVA) 14.2 vs 22,1% p = 0.001 with BMS and DES, respectively, Figure 3). We selected these three DES trials as

Table 3. Impact of type of stent in 11 randomized clinical trials and differences in baseline characteristics among them.

Type of Stent	PCI	CABG	p-value	Diabetes	3VD	Any LM
BMS (n = 3051)	8.7%	8.2%	p = 0.72	17.8%	41.9%	1.0%
First-generation DES (n = 4300)	13.2%	11.1%	p = 0.039	59.2%	69.4%	30.5%
New-generation DES (n = 3969)	10.3%	7.9%	p = 0.068	27.7%	77.2%	79%

3VD: Three-vessel disease; BMS: Bare metal stent; CABG: Coronary artery bypass graft; DES: Drug-eluting stent; LM: Left main coronary artery; PCI: Percutaneous coronary intervention. Date taken from [22].

comparison because they had available 5 years of follow-up results and angiographically their patient population included only a cohort of multiple vessel CAD [16,19,20].

Moreover, and of interest, in BMS versus CABG trials, [20] attrition rate beyond 1 year and up to 5 years have been similar with both revascularization techniques for the primary end point of death/MI/CVA 5.5 versus 5.5%, as well for death 5.5 and 5.4% or MI 0.8 and 0.6%, for PCI and CABG, respectively. When same analysis was performed in BEST trial, [8] death/MI/stroke were observed in 7.5 and 4.8% with PCI and CABG respectively meaning an increase incidence of 2.7% more events with DES-2 (death/.MI/CVA) beyond one-year. Furthermore, spontaneous MI beyond 30 days was <0.004 higher with PCI. Of note, in BEST trial [8] only patients with 2 or 3 vessel CAD were included.

Similar concerns arise if we look long-term follow-up outcome in EXCEL [10] and NOBLE [9] trials reflected by the incidence of spontaneous MI observed beyond 30 days. It was significantly higher than CABG arm (PCI 6.8% vs CABG 3.5% p < 0.001 and PCI 8% vs CABG 2.7% p = 0.0002 in EXCEL [10] and NOBLE [9] trials, respectively).

A recent meta-analysis from 5 RCT of DES versus CABG in patients with LMCA stenosis didn't find differences in death, cardiac death, MI or cerebrovascular accident (CVA) at the longest available follow-up. However, in our understanding this analysis had limitations, follow-up was different across trials, in three trials sample size was small and not powered to assess individual components of major end points, in SYNTAX trial LMCA patients was a subgroup of the entire cohort and more important in three of these studies, Boudriot, SYNTAX and PRE-COMBAT they used DES-1 designs who are now out of clinical practice because they reported unacceptable high number of stent thrombosis who was linked to cardiac death and MI [21]. Furthermore, Boudriot *et al.* [22] only reported 1 year of follow-up where comparative safety and effectiveness between DES and CABG was similar and is not the purpose of this revision. The only RCT showing comparative safety at 5 years between both revascularization strategies was PRE-COMBAT [11] who used an old sirolimus DES-1 design, in spite of authors find similar incidence of death and MI between both techniques, sample size was too small to address any conclusion and finding of this study was not replicate in any other DES versus CABG trials [23]. In fact, same authors reported significant differences in cardiac adverse events in the large registry among BMS, DES and CABG, MAIN COMPARE LMCA study, at 10 years of follow-up [24].

In summary after long-term follow-up of DES versus CABG randomized trials were completed in patients with MVCAD including LMCA, CABG reduce the incidence of death, MI, repeat revascularization and combined major adverse events [23].

What we have change with both revascularization strategies PCI and CABG in the last 15 years to achieve such divergencies in outcome between them?

Deep analysis of differences in long-term results with PCI & CABG in DES era

Differences in baseline characteristics are large enough to explained these findings

We can say that's statement is only partially true.

It's correct that there are baseline clinical and angiographic differences among BMS versus CABG and DES versus CABG trials, in terms of number of vessels, presence of diabetics, LMCA as is described in Tables 2 and 3.

However, these differences can't explain late attrition rate including incidence of spontaneous MI beyond one year observed in almost all DES RCT included registries [17,22]. This late attrition rates were also observed in the BEST trial [8] with a patient population quite similar to the old BMS trials. Furthermore, NOBLE trial [9] in where completeness of revascularization was similar between PCI and CABG (92 vs 95%, respectively; p = 0.54 Table 1), in spite of this achievement, number of spontaneous MI was significantly higher with DES suggesting that the

cardiac event could be developed by the stent itself. The advantage of CABG bypassing of long lesion segments which protects, to a greater extent, against target lesion MI and proximal *de novo* lesion MI were also described previously as an advantage of CABG over PCI, although, this hypothesis was not demonstrated in non-DES versus CABG RCT [4,5].

The Kaplan–Meier freedom from death/MI/CVA observed between 30 days to 5 years in BMS and CABG trials curves are complete superimpose, and significant different to those seen in current DES trials where after 1 year there is a continuous divergency in survival curve in favor to CABG mainly driving by the high incidence of spontaneous MI.

In summary, the answer to the first statement should be in spite of well-known baseline differences, there isn't a single reason responsible for the high rate of late adverse events after PCI with DES.

Stent thrombosis was almost gone after introduction of DES-2, however, spontaneous MI become a main concern to late patient outcome in modern PCI era

It has been well demonstrated after introduction of new polymers with latest DES designs, definitive, probable and possible stent thrombosis early or very late was significantly reducing its incidence and now safety of new DES designs are comparable or even better to the old BMS technology. Either new biocompatible polymers, polymers free stents, biodegradable polymers or very thin struts DES improved degree of covered stent struts in a very short time period after implantation, reducing inflammation and also late stent mal apposition [25,26]. All of these new enhancements significantly reduce the incidence of thrombotic events with latest DES designs and now they match safety to BMS.

However, in spite of these improvements, two major concerns with this technology remain: *early neo-atherosclerosis and endothelial dysfunction*, both are linked with incidence of adverse events after PCI. These complications, *early neo atherosclerosis and endothelial dysfunction*, are developed by the polymer but also by the local action of the immunosuppressive drug [27,28]. Even though *neo-atherosclerosis* was also seen with BMS technology, its occurrence happens later on usually after 7 years of stent implantation, in contrast with DES that usually happened more earlier soon after the first year.

Pathologic studies with DES technology demonstrated that *neo-atherosclerosis* is present with chromo cobalt biocompatible permanent polymer everolimus eluting stents [27].

Therefore, spontaneous MI beyond one year after DES deployment may be related to this phenomenon. Spontaneous MI, who isn't related to the initial procedure or repeat revascularization procedures, was associated with cardiac death and morbidity and was a matter of recent controversies [9,10].

It's also well known that *endothelial dysfunction* was associated with adverse cardiac events, although more recently was also associated with noncardiac serious adverse events including high incidence of solid tumours [28].

How we can minimize incidence of *early neo-atherosclerosis and endothelial dysfunction* with PCI?

If neo-atherosclerosis is developed by the polymer and the local action of immunosuppressive drug, it's much easy to improve the polymers than avoid the local action of immunosuppressive drugs who was the purpose and the soul of DES technology. However eventually, we can minimize this problem using new abluminal coated biodegradable polymers with low amount of immunosuppressive drug who target the endothelial surface of the lesion with significant less amount of drug. Clinical data of this novel DES technology at 5 years showed a paucity of increase rate of MI between 1 to 5 years of follow-up, in fact is these pooled data only 2% increase of MI between 1 and 5 years was reported [29–31].

Normalization of *endothelial dysfunction* with DES technology was initially observed with Bioabsorbable scaffolds (BRS), however, unfortunately, dysfunction of the endothelium was seen again at late outcome with this device and we don't know if with new BRS magnesium technology we will able to overcome this problem [32].

Old BMS technology appears it didn't have at the same period of time this late adverse effect including when we associated BMS with the use of oral immunosuppressive or anti-inflammatory agents, rapamycin, prednisone or colchicine, during a short period of time after PCI. However, the amount of information in this regard is limited to only seven small pilots RCT [33–38].

In summary, answer for the second statement, either *early neo-atherosclerosis nor endothelial dysfunction* could be related to the high incidence of late adverse cardiac and noncardiac events after DES.

An aggressive PCI strategy is responsible for these findings

The SYNTAX trial [7] was an ambitious study launched soon after introduction of DES technology who included patients with complex CAD anatomy, 3 vessel and LMCA.

In this study, PCI operators and trial investigators included intermediate lesions (50 to <70%) and small vessels as part of revascularization strategy. Therefore, multiple stent implantation was the rule and an aggressive PCI strategy was performed. In fact, mean stent length is this trial was over 88 mm [7,39].

Trial investigators in a *post hoc* analysis also build an angiographic risk score called Syntax Score (SS). This score was calculated by classifying eleven types of lesions: number of diseased segments, tortuosity, calcified lesion, thrombus, lesion length, dominance criteria, bifurcated and trifurcated lesions, ostial lesions, diffuse disease and CTO (chronic total occlusion) [40]. Intermediate lesions with stenosis of greater than or equal to 50% were included, in addition to including lesions in vessels greater than or equal to 1.5 mm. The SS was classified into three groups low SS with a score of up to 22 points, intermediate SS with points of 23 to 32, and a high SS of 33 points or more. Despite the fact that SYNTAX trial was not designed to express results between the SS groups, it was strongly concluded that patients with low SS can be treated with PCI or CABG, while in the intermediate or high SS they achieved more benefit with CABG. In spite of '*post hoc*' nature of SS, these observations were promptly included in revascularization guidelines [41]. Most of RCT with DES designs followed this aggressive approach as PCI strategy, in fact, if we look stent length in BEST trial it was 85.3 mm suggesting in spite of better stent design used in such trial PCI strategy was similar to SYNTAX trial [39] including in the revascularization strategy all intermediate lesions (50 to <70%) and lesions located in small vessels.

However, SS did not have any predictive value when patients were treated with CABG, and was not validated in others large randomized trials with DES such as FREEDOM, [16] BEST, [8] NOBLE [9] and EXCEL [10].

If *neo-atherosclerosis and endothelial dysfunction* are a cause of concern at long-term outcome and may be responsible for late adverse events, unnecessary multiple stent deployment, can be associate with poor long-term outcome.

ERACI risk score

The ERACI IV study [42] was a multicentre, observational and prospective registry with DES-2 in patients with multiple vessel CAD including LMCA stenosis. In this study investigators build up a new risk score, the ERACI risk score (ES) modifying original basal and residual SS [43]. Authors didn't include in the revascularization strategy either intermediate stenosis (<70%) or lesions located in small vessels defined as ≤2.0 mm visually estimated; accordingly, they were not scored. All other anatomic variables included in original SS, were incorporated and scored into ES. In ERACI IV, [42] using the original SS, 33.8, 32.4 and 33.8% of patients were included as low, intermediate or high, SS respectively. When we applied the ES low SS rose to 54.8%, intermediate dropped to 27.9% and only 17.2% of ERACI's patients scored as high SS Figure 4.

With this scoring, more patients are included within low or intermediate risk score changing risk profile and more patients could be candidates for PCI.

With this new risk assessment around 80% of patients with multiple vessel CAD can be treated with PCI . In EXCEL trial, [10] in whom only patients with a low and intermediate SS were allow to be included, around 24% of the population had finally a high SS by core lab assessment and these discrepancies between on site and core lab were mostly driven by the presence of lesions located in small vessel.

PCI strategy used and guided for this risk score, stenting stenosis ≥70% in large vessels (≥2.0 mm), was validated in ERACI IV study [42] using a second chromo cobalt generation DES-2 where at 3 years incidence of MI and progression of MI between first and third years was 1.8 and 1.4% significantly lower to DES-1 generation where was 6.2 and 3.5%, respectively, p = 0.01 in same study. In this registry combined DES-2 plus a conservative PCI strategy achieved a very low rate of adverse events up to 3 years of follow-up [44].

This study also showed a remarkable low rate of adverse events in initially nonstented lesions at 3 years, (3.6% of target lesion revascularization) supporting the policy of a conservative strategy with stent deployment during PCI.

In SYNTAX II 'guided' PCI [45] compared with SYNTAX I-PCI arm and in spite of SYNTAX II had less lesion treated per patient ($p < 0.001$) and less DES per patient implanted ($p < 0.001$) with similar SS. they found lower MACCE and MI rates as compared with SYNTAX I-PCI arm and similar to SYNTAX I-CABG arm Therefore, the results of SYNTAX II are in agreement and supported with those observed in ERACI IV.

In summary, if DES implantation has the risk to developed *neo-atherosclerosis*, unnecessary multiple stent implantation should be discarded and a *'conservative'* PCI policy is recommended.

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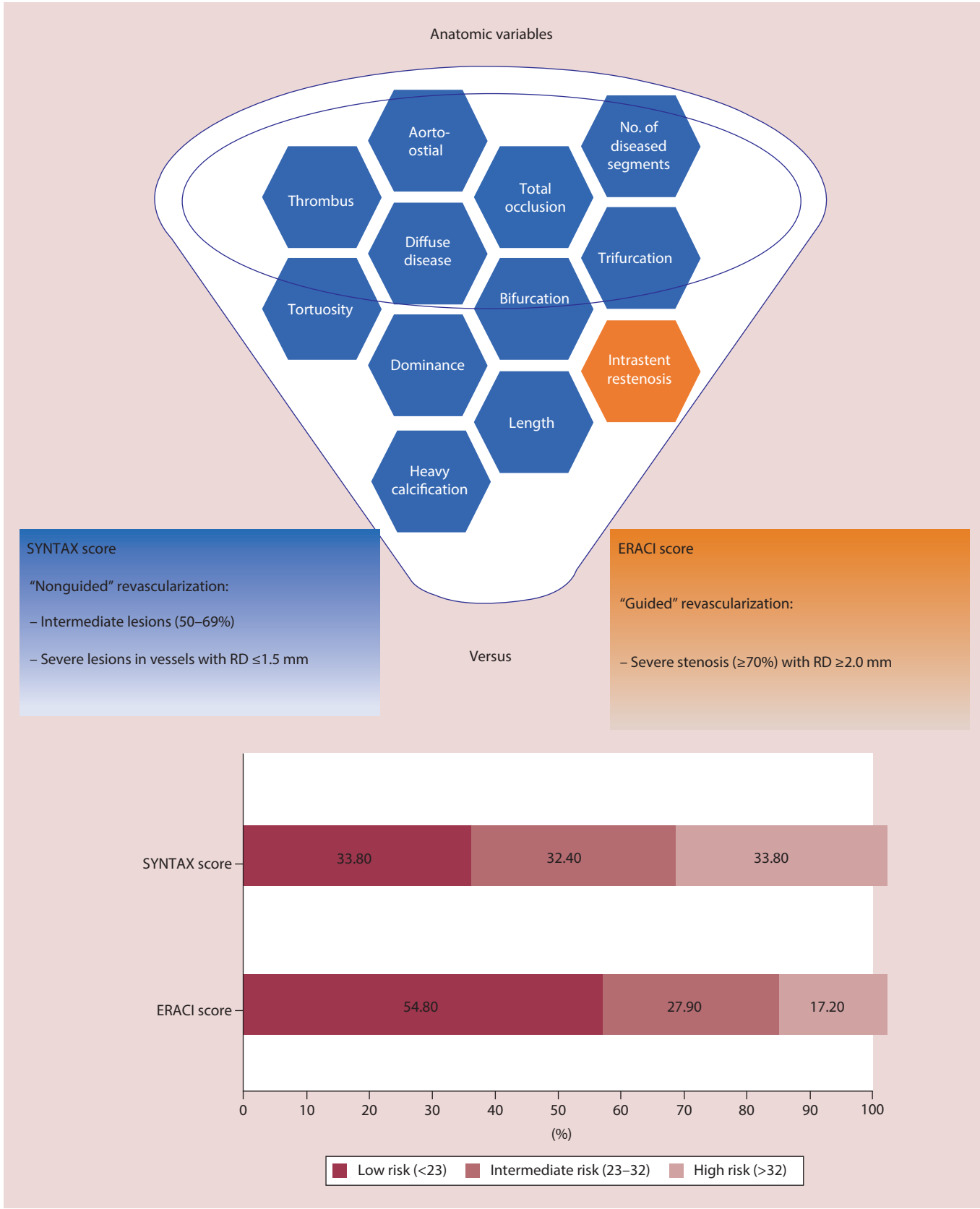

Figure 4. Stratification of patients using ERACI and SYNTAX scores.
RD: Reference diameter.
Data taken from [40,42–44].

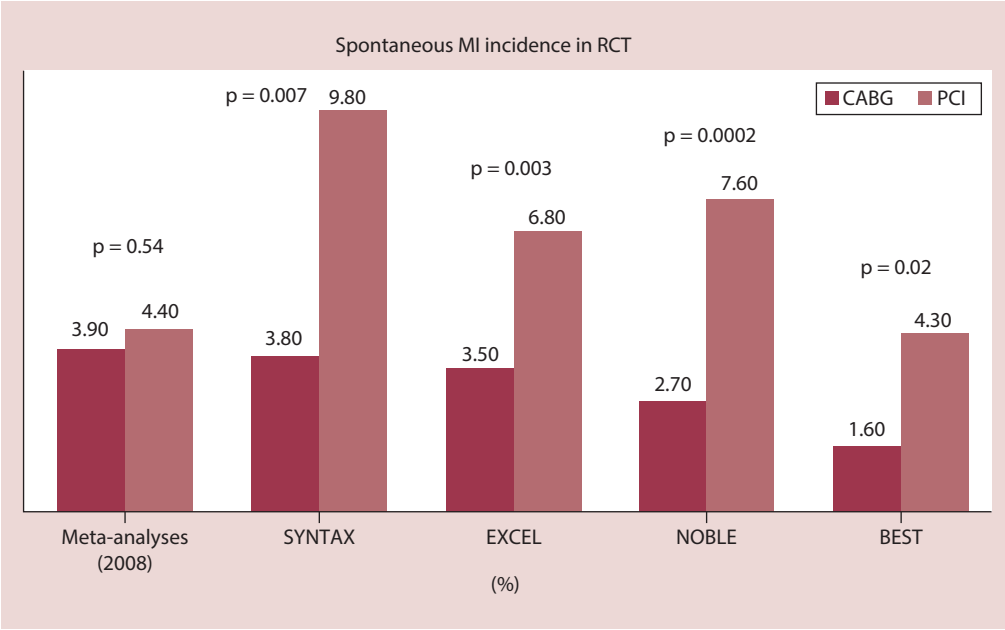

Figure 5. Spontaneous myocardial infarction incidence in randomized controlled trials and a meta-analysis.
CABG: Coronary artery bypass graft; MI: Myocardial infarction; PCI: Percutaneous coronary intervention; RCT: Randomized clinical trial.
Data taken from [7–10,16,19,20].

Improvement in the outcome is only seen with CABG

If we look the long-term results of CABG in RCT in the last 20 years, patients undergoing CABG as initial procedure have had an improvement in the outcome through the years in spite of differences in baseline risk profile.

In contrast to what happened with PCI arm, patients treated with CABG had a lower incidence of nonprocedural MI compared with those observed in old trials (Figure 5).

In the old BMS versus CABG trials, [20] CABG at 5 years had a nonprocedural incidence of MI of 3.9%, whereas at the same follow-up time in the DES versus CABG trials, CABG reported a MI incidence of 3.8% in SYNTAX, [7] 3.5% in EXCEL, [10] 2.7% in NOBLE [9] and 1.6% in BEST [8] meaning in spite of high baseline risk profile, CABG maintained or improved its long-term results Figure 5.

Better CABG technique with major utilization of multiple arterial conduits together with an improvement in medical therapies can explained these results.

Why these progresses in outcome are seen only in the CABG arm is the main purpose of this revision and at our understanding lack and/or delay in recognition of the problem will not allow us to find solutions.

High noncardiac mortality observed in EXCEL trial it happened by chance or is a cause of concern

We can't respond it appropriately with current available data.

However, in old meta-analysis from RCT between PCI versus CABG there was no mortality benefit with CABG at long-term outcome excluding diabetic patients [4,5].

That's was not the case in current era where there is a mortality benefit with CABG in diabetic and nondiabetic patients when we included all DES versus CABG trials at long term [19,22].

Differences in cardiac and noncardiac mortality was not analysed in the recent meta-analysis from 11 RCT conducted by Head *et al.*, [22] thus, we can only speculate possible reasons for this observation of high mortality in EXCEL trial [10] driving by a great incidence of noncardiac death.

Why a patient population with similar baseline characteristics will develop differences in mortality at 5 years?

First answer: because patients were treated with different revascularization procedures and one of them, CABG, had safety advantages over the other, but why the benefit is related to noncardiac instead cardiac mortality?

Second answer: because patients in PCI arm are taking more frequently medication linked to long-term noncardiac side effects such was reported with long-term DAPT therapy [18].

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Third answer: because DES develop *endothelial dysfunction* what was associated recently with noncardiac serious adverse events at long-term included solid tumors [28].

Fourth answer: because it happened by chance, the study was not powered to assessed mortality rate.

Fifth answer: because they were inappropriate assigned as noncardiac (unlikely).

Sixth answer: a combined of some or all of the above.

Future perspective

In spite of the use of latest DES designs, gap between PCI and CABG in modern DES-era was not narrowed in terms of serious cardiac late adverse events when we compared with old randomized data [4,5].

Major baseline angiographic differences could be one of the answers for these findings but clearly isn't the single one.

Presence of both *early neo-atherosclerosis and endothelial dysfunction* could be responsible for these late attrition rate observed beyond the first year in most of DES treated patients.

Less number of DES implanted per patient appears to be related with better outcome as was seen in recent observational studies [42,43,45].

The use of DES designs with less amount of immunosuppressive drug who targeting the lesion from abluminal endothelial surface could be one of the potential solutions for problems described here, some early data are supporting this hypothesis.

Lastly, we can't discard the use BMS technology associated with oral immunosuppressive or anti-inflammatory drugs to prevent repeat revascularization procedures during first year after PCI if advances of DES technology didn't find solutions to the main current concerns of this technology *early neo-atherosclerosis and endothelial dysfunction.*

Conclusion

Finally, and as take-home message, until we find out what would be the best strategy and the best device during PCI, it is recommended to don't perform any new randomized comparison against CABG. From 15 years to now PCI is losing most of randomized comparisons either with CABG [22] or medical therapy [46,47]. Consequently, numbers of PCI per year is continuous decreasing, [48] it's time to rethinking and rewrite what we done with PCI in the last 15 years and what will expect to leave to our fellows in the next 10 years to come.

Executive Summary

Deep analysis of differences in long-term results with percutaneous coronary intervention & coronary artery bypass graft

- There are differences in outcome among drug eluting stent (DES), bare metal stent (BMS) and coronary artery bypass graft (CABG) during different follow-up periods.
- During first year DES showed clear safety/efficacy advantages over BMS and CABG. Less target vessel revascularization-myocardial infarction compared with BMS and less 30 days death/MI and CVA compared with CABG.
- However, beyond first year we are seeing and attrition of efficacy of DES over the time to the extend we have not seen either with BMS or CABG. These disadvantages translated to poor overall outcome when compared with CABG.
- Therefore, we should need a percutaneous coronary intervention (PCI) strategy/stent design who combined safety/effectiveness of 1st year DES designs with late safety/effectiveness of old BMS designs.

The ERACI score

- The ERACI risk score modified the original SS, including in the scoring only severe lesions visually estimated (≥70%) in major epicardial vessels with a large jeopardized myocardial at-risk, therefore, they avoided to stent either small vessel or intermediate (50 to 70%) stenosis. With this approach, they can reclassify patients to a low or intermediate risk score allowing to more patients be candidates to PCI.
- Additionally, unnecessary multiple DES implantation has been associated with poor outcome [42,45].
- With this criterion, we can reduce late adverse events and more patients could be acceptable candidates to PCI instead to CABG in patients with multiple vessel CAD included LMCA stenosis.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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Papers of special note have been highlighted as: • of interest; •• of considerable interest

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