New insights in mechanism, diagnosis and treatment of myocardial infarction

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CHAPTER 5

LATE STENT MALAPPOSITION RISK IS HIGHER AFTER DRUG-ELUTING STENT COMPARED WITH BARE-METAL STENT IMPLANTATION AND ASSOCIATES WITH LATE STENT THROMBOSIS

ABSTRACT

Aims: Late stent malapposition (LSM) may be acquired (LASM) or persistent. LSM may play a role in patients who develop late stent thrombosis (ST). Our objective was to compare the risk of LASM in bare metal stents (BMS) with drug-eluting stents (DES) and to investigate the possible association of both acquired and persistent LSM with (very) late ST.

Methods and Results: We searched PubMed and other relevant sources from January 2002 to December 2007. Inclusion criteria were: (a) intra-vascular ultrasonography (IVUS) at both post-stent implantation and follow-up; (b) 6 – 9 months follow-up IVUS; (c) implantation of either BMS or the following DES: sirolimus, paclitaxel, everolimus or zotarolimus; and (d) follow-up for LSM. Of 33 articles retrieved for detailed evaluation, 17 met the inclusion criteria. The risk of LASM in patients with DES was four times higher compared with BMS (OR= 4.36, CI 95% 1.74 – 10.94) in randomized clinical trials. The risk of (very) late ST in patients with LSM (five studies) was higher compared to the patients without LSM (OR= 6.51, CI 95% 1.34 – 34.91).

Conclusion: In our meta-analysis, the risk of LASM is strongly increased after DES implantation compared with BMS. Furthermore, LSM seems to be associated with late and very late ST.

Keywords: Meta-analysis; Late stent malapposition; Late stent thrombosis; Drug-eluting stents.

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INTRODUCTION

Late and very late stent thrombosis (STs) are rare,[1-5] but potentially lethal complications emerged during the increasing use of stent implantation. It was recently suggested that stent malapposition (SM) as assessed by intra-vascular ultrasonography (IVUS) imaging plays an important role in patients who develop very late ST after drug-eluting stent (DES) implantation.[6] SM (synonymous with incomplete stent apposition) represents a separation of at least one stent strut from the intimal surface of the arterial wall (in the absence of a side branch) with evidence of blood behind the strut.[7] SM can be acute if detected post-procedural, or late if detected at follow-up IVUS imaging.[8] Acute SM can resolve or persist during the follow-up period. Late SM (LSM) may be persistent if present both immediately after the procedure and at follow-up, or acquired if present only at follow-up (LASM).[9] Acute SM can generally be controlled by performing an IVUS immediately post-procedure and treated with subsequent balloon angioplasty. However, for LASM this is not the case as by definition there is no SM at the time of stent placement. Thus far, no clear conclusion could be drawn with regard to the occurrence of LSM (acquired or persistent) and the risk of (very) late ST as only a small number of studies report on LSM and its possible relation with ST and the incidence of (very) late ST is relatively low. Therefore we have conducted a meta-analysis to compare the risk of LASM between bare-metal stents (BMS) and drug-eluting stents (DES) and a sub-analysis to investigate the possible association of LSM (acquired or persistent) with (very) late ST.

METHODS

Selection of studies

We searched PubMed, Web of Science, Embase, and the Cochrane Central Register of Controlled Trials between January 2002 and December 17, 2007 with the keywords

(IVUS OR intravascular ultrasonography OR interventional ultrasonography OR intravascular ultrasound OR intravascular ultrasonic) AND (Cypher OR SES OR Sirolimus OR Endeavor OR ABT-578 OR Promus OR Everolimus OR Taxus OR Paclitaxel OR DES OR drug-eluting stent OR drug-eluting stents OR drug eluted stent OR drug eluted stents OR BMS OR bare-metal stent OR bare-metal stents) or variants of these terms, adapted to each of the different databases. Relevant websites (http://www.tctmd.com, www.europcr.com, www.acc.org, www.theheart.org, www.escardio.org and www.clinicaltrialresults.org) were searched for pertinent abstracts and expert slides presentations. No language restriction was applied.

To be selected for this meta-analysis, studies had to meet the following criteria: (a) IVUS analysis in native coronary arteries at both baseline and follow-up; (b) follow-up IVUS performed no sooner than 6 months and not later than 9 months after stent implantation; (c) implantation of either BMS or one of the following DES: sirolimus-,

paclitaxel-, everolimus- or zotarolimus-eluting stents; (d) recording of late stent malapposition. For the analysis of late ST risk in LSM patients, we searched among the included papers those that presented follow-up data for ST in two separate groups: LSM vs. non-LSM.

Data abstraction

Two investigators (A.K.M.H. and S.C.B.) independently extracted all data, and disagreements were solved in consultation with a third investigator (J.W.M.P.). A number of 221 papers were identified from PubMed, 71 papers from Web of Science and EMBASE and 3 additional clinical trials from relevant websites (total of 295 citations) (Figure 1).

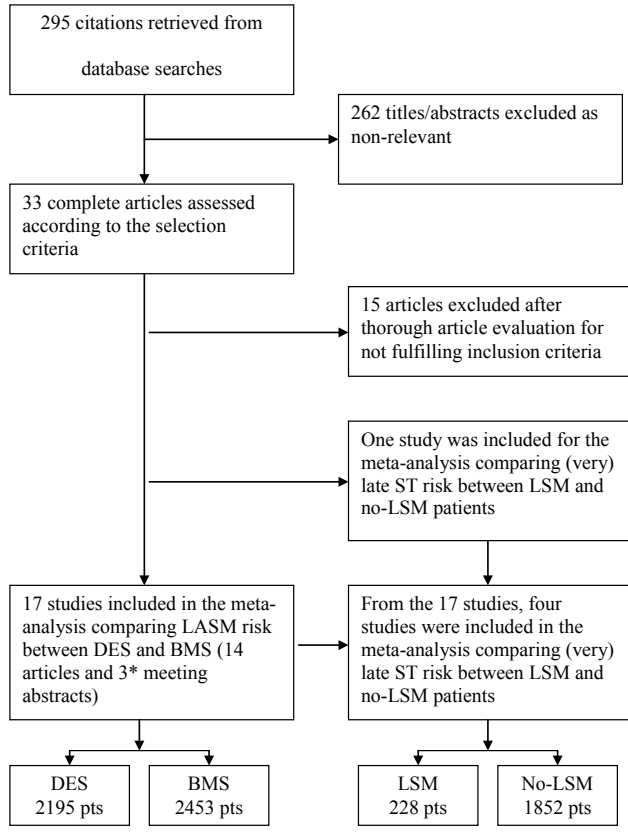

Figure 1. Flow diagram of the review process. Process of identification and selection of studies for inclusion in meta-analysis. BMS, bare metal stents; DES, drug eluting stents; LASM, late-acquired stent malapposition; LSM, late stent malapposition (acquired or persistent); pts, number of patients; ST, stent thrombosis. *Data for the MISSION! Study was initially collected from expert presentation. Before submission, the results were published and were therefore added a reference[35] for an easy access of the reader.

After reading the titles and abstracts, we identified a potential number of 33 papers from which 17 studies were eligible for inclusion. Among these, nine papers presented original results from randomised clinical trials (RCTs) that compared DES with bare metal stents BMS. We searched among the references from the identified studies and from most recent review articles on DES for relevant papers, but no further studies were identified. Five papers that provided data on the incidence of ST in patients with LSM (acquired or persistent) were used for the assessment of late ST risk. Data were extracted from studies as they were presented. The authors did not review individual patients' data and therefore special attention was paid to avoid repeated analysis of same data (as this may arise when same core laboratories publish multiple studies).

Drug eluting stents

Two major categories of DES are described in our study: the "-limus" group comprising sirolimus, everolimus and zotarolimus, and the paclitaxel group.

The "-limus" group prototype is rapamycin (sirolimus), a macrolide with cytostatic properties that blocks progression from G1 to S in the cell cycle and inhibits thus the vascular smooth muscle cell migration and proliferation.[10,11] The newer generation rapamycin derivative everolimus[12,13] is reported to be more lipophilic than sirolimus whereas zotarolimus[14,15] efficiently suppresses the lymphocyte-mediated local inflammatory reaction. Paclitaxel inhibits vascular smooth muscle cell migration and proliferation mainly as a result of binding to and stabilizing cellular microtubules.[10,16]

The construction of the sirolimus-eluting stent (SES, CYPHER™), paclitaxel-eluting stent (PES, TAXUS EXPRESS™), everolimus-eluting stent (EES, XIENCE V™/PROMUS™) and zotarolimus-eluting stent (ZES, ENDEAVOR™) is described elsewhere.[10-16]

IVUS imaging and analysis

The IVUS acquisition and analysis technique was similar in all studies. After administration of intracoronary nitroglycerin, IVUS images were acquired using commercially available imaging systems with automated transducer (0.5 mm/s). Images were acquired for every mm in the stent and for 5 mm proximal and distal of the stent and were analyzed with various commercially available software. LASM assessment was performed as follows. First, investigators reviewed all follow-up IVUS recordings to identify cases of SM. Secondly, in identified cases, immediate post-stenting and follow-up IVUS images were reviewed side-by-side to discriminate cases in which SM existed immediately after stent implantation or not.

SM was defined as one or more stent struts clearly separated from the vessel wall with evidence of blood speckles behind the strut in a vessel segment not associated with any side branches.[7]

Statistical analysis

To compare BMS with DES, two analyses were performed. The first was based on all 17 studies included in the meta-analysis (Table 1).

The second analysis was restricted to the seven studies that compared BMS with DES in a randomised manner. The first analysis was based on the bivariate-random effects model as described by Van Houwelingen et al.[17] In this model also the studies with only one treatment group, BMS or DES, are used. Owing to the small number of patients with LASM, the usual normal approximation for the number of events within a treatment group is not reliable, and the exact binomial distribution was used instead, as described by Chu and Cole.[18] The second analysis was based on a standard random-effects model for the log odds ratio. However, due to the small numbers of LASMs, the hypergeometric distribution as described by van Houwelingen et al.[19] was used to model the number of events within a study, instead of the usual normal approximation. A third analysis was performed to compare the '-limus' group of DES with the paclitxel group. There were only three studies directly comparing a '-limus' stent with PES. However, six studies compared '-limus' with BMS and three studies compared PES with BMS. These studies contain indirect evidence on the comparison of '-limus' with PES. To combine all the evidence on this comparison, a tri-variate meta-analysis was performed as in Arends et al.,[20] assuming compound symmetry for the covariance matrix of the random effects. To accommodate the small numbers of LASMs, again the exact binomial distribution was used to model the number of events within a treatment group. A fourth analysis was performed to compare the incidence of late ST between patients with and without LSM. As stated, there were only five studies providing data on this comparison, and the numbers of late ST were very small, prohibiting a random effects meta-analysis. Therefore we used a fixed effects analysis using the exact Mantel-Haenszel test. We provide in Table 2 the expected values of (very) late ST under the assumption of the null hypothesis [LSM is not related to (very) late ST]. All analyses were performed using the SAS statistical package version 9.1.3. The procedure Proc NLMIXED was used for the random-effect meta-analyses.

Study quality assessment

As mentioned earlier, our meta-analysis was especially designed to extract data from various types of available studies: observational studies in which the authors present the incidence of LASM within BMS or DES cohorts; RCTs in which two types of DES are compared; RCTs in which BMS is compared in a randomized manner with BMS after rotablation and RCTs where DES are compared to BMS. Only for the latter category it is of interest to perform an RCT study quality assessment. We have used the Delphi list for quality assessment of randomized clinical trials as described by Verhagen et al.[21]. In short, the Delphi list allocates "yes", "no" or "do not know" to a total number of 9 questions. Quality of RCTs is defined as the likelihood of the trial design to generate unbiased results. When five or more questions are answered "yes'

the RCT is considered to have a low risk of bias. In a respective manner, RCTs may have unclear or high risk to cause bias.

RESULTS

Search results and study characteristics

A total of 17 studies[22-38] with 4648 patients were included in this meta-analysis (Table 1).

A number of 2453 patients received BMS and 2195 received DES. The mean age of the participants in individual trials varied from 56 to 67 years. The mean timepoint of IVUS follow-up ranged from 6 to 9 months. Eleven trials [22-24,26,27,30,31,33-35,37] represent data from randomized control trials (RCT). Among these, 9 studies [22,24,26,27,30,33-35,37] analyzed DES versus BMS (944 patients with BMS and 1050 patients with DES), one study randomized two types of DES[23] and one study randomized only BMS with or without prior directional coronary atherectomy (DCA). [31]

Among the whole analyzed group, SES appeared in four studies,[22,25,30,35] PES in four studies,[24,27,33,37] EES in one study,[34] and ZES in two studies.[26,36] Three trials compared two different types of DES (SES vs PES[29,38] and EES vs PES[23]), while the remaining three studies included BMS only.[28,31,32]

The incidence of LASM in patients treated with DES varied with the type of stent used: the highest incidence was observed in SES (4%,[25,38] 9%,[22] 13%,[29] 15%,[30] 25%[35]) followed by PES (2%,[23,27] 5%,[24] 8%,[29,37] 9%,[33] 15%[38]) then ZES (0%[26] to 7%[36]) and the lowest incidence was observed in EES (0%[34] to 1%[23]). LASM was observed in 0 – 6% of the patients treated with BMS.[28,31,32]

Risk of late-acquired stent malapposition in drug-eluting vs. bare-metal stents

The incidence of LASM varied between DES and BMS: (a) in DES, the highest incidence was 25% at 9 months in the MISSION! Intervention Study[35] while the lowest incidence was 0% at 6 months[34] and 8 month;[26] (b) in BMS, the highest reported incidence was 6% at 6 months[28] whereas the lowest incidence was 0 % at 6 months,[25,27,34] 8 months[22,26] and 9 months.[30]

In our meta-analysis, the pooled odds ratio varied according to the approach we used. When both randomized trials and all observational studies were included,[22-38] the risk of LASM in patients with DES was 2.5 times higher compared to those with BMS (OR= 2.49, CI 95% 1.15 – 5.35, P= 0.02). When we included in our meta-analysis only the randomised controlled studies comparing DES with BMS (seven randomized control studies[22,24,27,30,33,35,37] were included and two remaining studies[26,34] reported zero cases in both arms), the risk of LASM in patients with DES was four times higher compared to those with BMS (OR= 4.36, CI 95% 1.74 – 10.94, P= 0.002). (Figure 2).

Table 1. Characteristics of the source studies.

Study	Design	Mean age (years)	Men (%)	Diabetes mellitus (%)	Inclusion criteria	Follow-up (months)	Stent	No. of patients	No. of LASM
Ako et al , 2005 (SIRIUS)[22]	RCT	62	72	26	SA/UA/signs of myocardial ischemia	8	SES	80	7
							BMS	61	0
Van der Hoeven et al, 2007 (MISSION!)[35]	RCT	59	78	10	STEMI	9	SES	104	26
							BMS	80	4
Jiménez-Quevedo et al, 2006 (DIABETES)[30]	RCT	67	62	100	Symptoms or objective evidence of ischemia	9	SES	75	11
							BMS	65	0
Tanabe et al, 2005 (TAXUS II)[33]	RCT	62	76	15	SA/UA/SI	6	PES	229	20
							BMS	240	13
Chechi et al, 2007 (SELECTION)[24]	RCT	60	82	13	AMI	7	PES	39	2
							BMS	37	1
Weissman et al, 2007 (TAXUS IV, V, and VI)[37]	RCT	62§	72	28	SA/UA/SI	9	PES	287	24
							BMS	260	9
Hong et al, 2003 (ASPECT)[27]	RCT	59	75	14	Symptomatic coronary heart disease	6	PES-NP*	56	1
							BMS	25	0
Bullesfeld et al , 2007 (SPIRIT III)[23†]	RCT	63	67	29	SA/UA/SI	8	EES	90	1
							PES	43	1
Tsuchiya et al, 2006 (FUTURE I ,II)[34]	RCT	65	80	12	SA/UA/SI	6	EES	48	0
							BMS	58	0

Fajadet et al, 2006 (ENDEAVOR II)[26]	RCT	62	76	20	Symptoms or objective evidence of ischemia	8	ZES	132	0
							BMS	118	0
Nakamura et al, 2003 (DESIRE)[31]	RCT	62	85	NA	NA	6	BMS	412	10
Hong et al, 2006 [29†]	OS	57	73	23	SA/UA/AMI	6	SES	538	71
							PES	167	14
Degertekin et al, 2003[25]	OS	61	76	4	SA/UA/SI	6	SES	24	1
							BMS	10	0
Siqueira et al, 2007[38]	OS	60	68	46	SA/UA	8	SES	175	7
							PES	20	3
Hong et al, 2004[28]	OS	56	75	21	SA/UA/AMI	6	BMS	881	54
Shah et al, 2002[32]	OS	57	100	1	SA/UA/SI	6	BMS	206	9
Waseda et al, 2007 (ENDEAVOR RESOLUTE)[36]	OS	61	75	18	SA/UA/SI	9	ZES	88	6

AMI, acute myocardial infarction; BMS, bare metal stent; EES, everolimus eluting stent; LSM, late stent malapposition; NA, not available; OS, observational study; PES, paclitaxel eluting stent; RCT, randomized control trial; SES, sirolimus eluting stent; SA, stable angina; SI, silent ischemia; STEMI, ST-segment elevation myocardial infarction; UA, unstable angina; ZES, zotarolimus eluting stent; *non-polymer-encapsulated paclitaxel-coated stents; [†]we considered number of lesions equal to the number of patients; [§]Only IVUS groups.

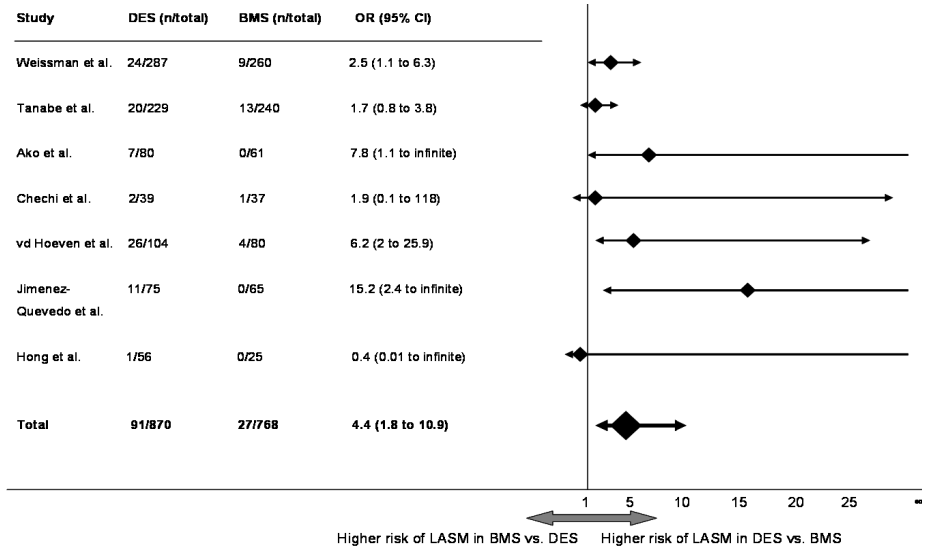

Figure 2. Odds ratio (95% CI) for late-acquired stent malapposition in drug-eluting stent versus bare-metal stent in individual trials; Squares, odds ratios (OR); lines, 95% confidence intervals (95%CI); n, number of patients with late acquired stent malapposition; total, total number of patients in each stent group; BMS, bare metal stents; DES, drug eluting stents; LASM, late acquired stent malapposition; ∞, infinite.

Risk of late-acquired stent malapposition in patients with paclitaxel-eluting stents compared with "-limus"-eluting stents

The meta-analysis comparing paclitaxel with '-limus' eluting stents showed that the risk of LASM was not significantly (OR = 0.84, 95% CI 0.26 – 2.71, P = 0.77) lower after paclitaxel-eluting stent implantation.

Risk of (very) late stent thrombosis in patients with late stent malapposition (acquired or persistent)

In our meta-analysis we used 5 studies[33,37-40] to calculate the risk of late ST in patients with LSM (n= 228) compared with patients with no LSM (n= 1852). We demonstrate that the risk of (very) late ST in patients with LSM was higher compared to patients without LSM (OR= 6.51, CI 95% 1.34 – 34.91, P= 0.02). (Table 2)

Based on the expected numbers of (very) late ST, there are three trials[38-40] in favour of the relation between LSM and ST , and two studies[33,37] with a slight tendency not to support this relation.

The recommended length of thienopyridine therapy after stent implantation was highly variable between the studies: 2 to 3 months in Hoffman et al.,[39] 6 months in Tanabe et al., and Weissman et al.,[33,37], 6 months in Hong et al.[29,40] (however 60% of his patients received additional 5 month of treatment after the original 6-month follow-up), 3 – 6 months in Siqueira et al.[38] and 12 months in van der Hoeven et al.[35]

Table 2. Characteristics of the studies used for assessment of the risk of (very) late stent thrombosis in patients with and without late stent malapposition

Study	Design	Clinical Follow-up (months)	Type of stent	LSM	Patients number	Observed values for (very) late ST		Expected values for (very) late ST	Definition of ST
						Late ST (≤ 12 months)	Very late ST (> 12 months)		
Hoffmann et al.[39]	RCT	48	SES+BMS	YES	57	0	1	0.18	Occurrence of acute symptoms in combination with angiographically documented TIMI flow 0 or 1 or the presence of flow-limiting thrombus (TIMI flow 1 or 2)
				NO	268	0	0	0.82	
Tanabe et al.[33]	RCT	12	PES+BMS	YES	46	0	NA	0.20	NA
				NO	423	2	NA	1.80	
Hong et al.[40]	OS	36	SES+PES	YES	82	NA	1	0.44	According to the Academic Research Consortium Criteria [48]
				NO	475	NA	2	2.56	
Siqueira et al.[38]	OS	29†	SES+PES	YES	10	0	2	0.11	Angiographic documentation of partial or total stent occlusion with or without the presence of thrombus and sudden cardiac death or MI that is not clearly attributable to another coronary lesion
				NO	172	0	0	1.89	
Weissman et al.[37]	RCT	24	PES +BMS	YES	33	0	0	0.06	NA
				NO	514	1	0	0.94	

BMS, bare metal stents; LSM, late stent malapposition; MI, myocardial infarction; NA, not available; OS, observational study; RCT, randomized control trial; ST, stent thrombosis; SES, sirolimus eluting stent; PES, paclitaxel eluting stent; † Mean duration of clinical follow-up

Randomized clinical trials quality assessment

Each of the RCTs comparing DES with BMS (seven randomized control studies[22,24,27,30,33,35,37] used in the analysis presented in Figure 2) had five or more questions answered with "yes" when assessed with the Delphi list. Therefore all seven RCTs were considered to have a low risk of introducing bias in the assessment of LASM in DES vs. BMS.

5 DISCUSSION

Our key findings were: (a) the risk of LASM was significantly higher after DES versus BMS implantation; (b) the risk of LASM does not differ significantly between paclitaxel- and "-limus"-eluting stents and (c) the presence of late (acquired or persistent) SM at follow-up was significantly associated with the risk of developing (very) late ST.

Late acquired stent malapposition

In our meta-analysis, the risk of developing LASM in all observational and randomized trials appeared to be slightly lower than in the RCTs only (odds ratio= 2.5 vs. 4.4, respectively). These results may be interpreted from the perspective that each RCT used in the RCT-only analysis was assessed (as described in Methods section) to have low risk of inducing bias in the meta-analysis, in which no similar formal quality assessment may be performed to the rest of the studies included in all observational and randomized trials analysis. The highest incidence of LASM in the DES group was observed in studies including patients with acute myocardial infarction (MI), [35] unstable angina[38] and diabetic patients.[30] Independent predictors of LASM after BMS implantation were primary stenting in acute MI and DCA before stenting.[28,31] Tanabe et al.[33] also identified lesion length, unstable angina and absence of diabetes as predictive factors of LASM independent of BMS or DES use.

Two mechanisms for LASM were described both for BMS and DES[6,28,32,35,41]: decrease of the plaque volume behind the stent (including clot lysis or plaque regression) and positive remodelling of the vessel wall.

We found a higher risk of LASM in DES when compared with BMS. This difference could be attributable to the adverse effect of the drug on the vessel wall, resulting in positive remodeling.[35] Virmani et al.[42] reported that in BMS, hypersensitivity to the metallic stent was mostly associated with restenosis, whereas in DES, the hypersensitivity to the metallic stent, the polymer or to the drug was associated with positive remodelling and excessive inflammation in the vessel wall. Pires et al.[43] suggested that the vascular response to the DES in murine model differ with the type of drug used . This is also reported by Hong et al.[29] who compared SES and PES and suggested that the mechanism of SM in SES was a greater suppression of peri-stent neointimal hyperplasia whereas in PES, a greater amount of peri-stent positive remodeling was observed.

In our meta-analysis we looked for difference in the risk of LASM between different types of DES. Although there appeared to be a slightly lower risk in the PES group compared to '-limus' group, this was far from statistical significance.

Relation between stent thrombosis and malapposition

The present study suggests that the risk of (very) late ST in patients with LSM is higher compared to patients without LSM. Our results are consistent with a number of studies[6,44,45] suggesting LSM to be linked to (very) late ST. Other IVUS studies with BMS[27] and DES[22,29,33] failed this far to identify LSM as a predictor of clinical adverse events. However, the predictive accuracy of these studies was limited by a small number of patients with LSM (13 – 90 patients), the limited follow-up period of only one year after DES implantation, and the infrequent occurrence of (very) late ST.[6] In our meta-analysis, the real number of patients with late ST due to LSM may possibly be underestimated due to the fact that IVUS imaging was not performed before 6 to 9 months after implantation.

The mechanism by which LSM may contribute to ST remains unclear. It has been stated that SM may serve as a local nidus for thrombus formation by allowing fibrin and platelet deposition.[46] Moreover, SM may be the consequence of chronic inflammation and delayed healing resulting in tissue necrosis and erosion around the stent.[47] Delayed re-endothelialization, impaired vasomotion, and chronic inflammation may be as well regarded as primary ST mechanisms (SM being just a marker) by allowing the platelet adhesion, initiation of the coagulation cascade, and subsequent thrombotic stent occlusion.[6]

To the best of our knowledge, this is the first meta-analysis to assess the risk of LASM in DES compared to BMS. Furthermore we conducted an analysis on the risk of (very) late ST in patients with LSM. On the basis of the available data, LASM appears to be a problem that cannot be avoided by IVUS immediately after the procedure, that occurs more frequent with DES implantation, and is associated with increased risk of late and very late ST. Our findings demand a careful assessment of the intervention strategy and post intervention medical treatment as we may trade a benign complication of restenosis in BMS with the serious LASM and the subsequent ST in DES.

For the time being we do not know whether the presence of LSM should be treated and how. As it is evident that many LSMs may persist for years without leading to (very) late ST, we need to explore the underlying relation between LSM and ST and for how long should patients receive thienopyridine therapy after drug-eluting stent implantation. All these questions are to be clarified in future larger studies.

Limitations

Our results are not a substitute for a large RCT. All studies used in this meta-analysis included clear definition for LASM, except for one[39] in which the distinction between late acquired and persistent SM was not clear (the authors used data from the

RAVEL trial which did not have a post-procedural IVUS assessment). All analyzed studies reported the number of patients with LASM except for 2 studies[23,29] that reported the number of lesions instead of number of patients. For these studies we considered number of reported lesions to be equivalent to patients. For the (very) late ST subanalysis, the main limitation is the overall small number of patients with events. Another inconvenient is represented by the various definitions of ST. Ideally, an analysis structuring ST as definite, definite and probable and definite, probable and possible would grant the most reliable results. The present study does not provide any information on the relation between antiplatelet therapy and ST in the presence or absence of SM. However, we did not intend to perform a meta-analysis on the ST issue but a subanalysis investigating a possible relation between LSM and (very) late ST within the studies included in our main analyses. Therefore we consider that the hypothesis-generating purpose of this sub-analysis was accomplished. Consequently, future large and well-designed studies are warranted to replicate these findings.

The aim of the present meta-analysis was to investigate the outcome of stent implantation at a follow-up period no longer than 9 months. However, SM is a dynamic phenomenon and the absence of SM at IVUS follow-up does not warrant a well-apposed stent at later stages as well as it does not warrant a clinically uneventful course. We cannot exclude that these limitations may have influenced our results.

CONCLUSION

In our meta-analysis, the risk of LASM is strongly increased after DES compared to BMS implantation. Furthermore, LSM appears to be associated with late and very ST.
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CONFLICT OF INTEREST

none declared

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