Innovative therapies for optimizing outcomes of coronary artery disease

Ahmed, T.A.H.N.

Chapter 7

(Late) Stent Malapposition in the BMS and DES Era

Jeffrey J.W. Verschuren, MD[1]; Tarek A.N. Ahmed, MD[1]; Joannis Karalis, MD[1]; Paul H.A. Quax, MD, PhD[2, 3]; J.Wouter Jukema, MD, PhD[1, 3]

[1] Department of Cardiology, Leiden University Medical Center, Leiden, the Netherlands

[2] Department of Surgery, Leiden University Medical Center, Leiden, The Netherlands

[3] Einthoven Laboratory for Experimental Vascular Medicine, Leiden University Medical Center, Leiden, The Netherlands

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INTRODUCTION

Since the introduction of drug eluting stents (DES), the incidence of coronary stent restenosis has been significantly reduced. However, the safety of DES became a major issue after several studies associated DES with an increased risk of the rare but often devastating development of late and very late stent thrombosis [1-3]. Several risk factors have emerged as being important in the development of stent thrombosis, including stent malapposition. Although it is still under debate what the exact role of stent malapposition in this respect is, it appears undeniable that stent malapposition is involved in the development of this severe complication after stent implantation in at least a part of the cases [4-10].
In this chapter several aspects of stent malapposition will be discussed.

DEFINITION AND CLASSIFICATION

Stent malapposition (SM), also known as incomplete stent apposition, is defined by a separation of at least one stent strut from the intimal surface of the arterial wall with evidence of blood behind the strut, without involvement of side branches [11]. Stent malapposition may increase the thrombotic risk due to the presence of intraluminal stent struts [12]. Although appropriate apposition of the stent to the vessel wall is an important aspect for all stents, it seems to be critical in the case of DESs to ensure antiproliferative drug delivery as well as circumferential vascular support.
Depending on the time point of detection, the following classification can be made; acute if present immediately after the index procedure and late if detected at follow-up.
Furthermore, resolved if present after stent implantation but not at follow up, persistent if present both directly after stent implantation and at follow up and as acquired when the stent is well apposed after the index procedure but SM is detected at follow up. Differentiating between the different forms of SM therefore requires intravascular imaging both at stent implantation and at follow up. Schematically this is shown below as depicted by Hur et al., Cardiovasc Revasc Med 2009 [13].(Figure 1)
It is important to realize that the distinction between acute and late SM also implies different pathogenetic mechanisms for these two entities. Furthermore, each form will require a different therapeutic approach, which will be addressed later in the chapter.

PATHOPHYSIOLOGY

The current thought is that acute SM is mostly technique dependent and may result from inadequately sized stent selection or inadequate stent expansion, whereas late acquired SM

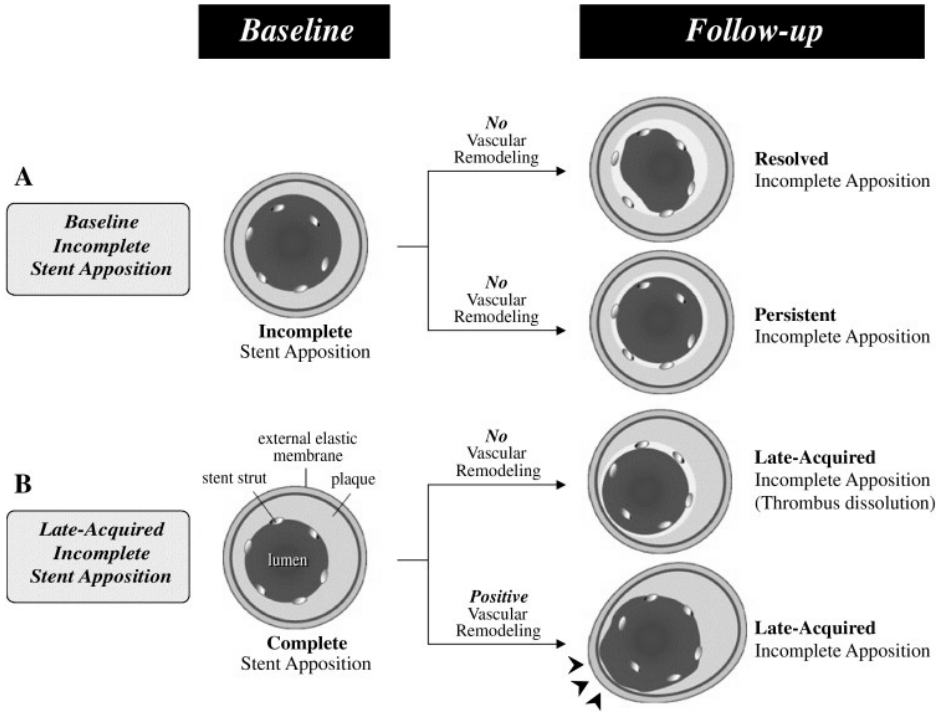

Figure 1. Various types of stent malapposition by Hur et al., Cardiovasc Revasc Med 2009. [13]

may result from vessel wall changes in the stented segments that occur during the follow-up period.

Focusing on late SM, several mechanisms have been postulated;[1] positive vascular remodeling of the vessel wall;[2] decrease in plaque volume;[3] chronic stent recoil and[4] a hypersensitivity reaction to one of the stent constituents.

Positive remodeling is the increase in vascular dimension measured by intravascular imaging using intravascular ultrasound (IVUS) or optical coherence tomography (OCT) by analyzing the change in cross sectional area of the external elastic membrane (EEM) in comparison with the change in plaque volume over time. Several studies reported a greater increase of the EEM compared to the change in plaque volume. Since the size of the stent cannot increase over time, except for the now rarely used self expanding stents, this process will eventually lead to stent malapposition [13-19]. A recent study of Kang et al. used IVUS immediately after intervention and at the 6-month and 2-year of follow-up to evaluate serial vascular changes after DES implantation [19]. Their main conclusion was that the development of malapposition was not limited to the first 6 months after implantation as a result of ongoing vascular remodeling even after this period. Therefore, the reported incidence of acquired late SM in previous studies (between 0% and 25% [20]) maybe underestimated due to relative short-term follow-up periods [19].

Besides an increase of the vascular dimensions, another possible mechanism to stent malapposition is a decrease of the plaque volume. This can be caused by dissolution of a thrombus, present at the stent implantation, mainly seen in patients with acute myocardial infarction [4, 13, 14, 21, 22]. Furthermore, regression of the plaque under stringent statin treatment can result in creating space between the stent and the vessel wall; however this seems to be only the case in a minority of lesions [12, 21, 23].

The pattern of late acquired SM is usually focal and is more often found at the borders of the stents (up to 90%, as reported by Mintz et al.)[17]. Additionally, acquired SM is more likely to occur in the relatively disease-free side of the vessel wall, probably because the normal vessel gets more injured during DES implantation and the delayed healing due to the drugs loaded on these stents [13, 24] . It is therefore more likely that positive remodeling is the most important mechanism for the development of late SM and that the contribution of plaque change is more limited [13]. Although chronic stent recoil could theoretically be one of the causes of SM, it has not been detected using IVUS in patients with SM, making it therefore unlikely to be a factor in the development of SM [17, 25].

Another factor of possible influence is the inflammatory response to these stents. In contrast to bare-metal stents (BMS), DES provokes inflammatory responses in animal models, either by a local hypersensitivity reaction to the non-biodegradable polymers of the stent or to the drug released by the stent. Since in a pig model the hypersensitivity reaction only peaks after complete release of the drug, it appears more likely that the polymer is the cause [22]. Also in human thrombectomy specimens, histopathological signs of inflammation were found, thus supporting the theory that a hypersensitivity reaction underlies the development of SM and stent thrombosis [5]. Furthermore, a growing number of reports documented the formation of coronary artery aneurysm (CAA) after DES implantation. Although the exact mechanism is still unknown, the available evidence suggest that it may be a hypersensitivity-mediated reaction to the delivery polymer [26]. Studies of related polymers have demonstrated local and systemic hypersensitivity reactions to intravascular polymers [5, 27-29]. Also, animal studies of DES show that 25% of pigs receiving DES develop eosinophilic infiltrates [29]. Bare-metal stents have not been demonstrated to elicit such hypersensitivity reactions in human autopsy series of over 400 stents [29].

RISK FACTORS

Predictors of acute SM include aneurysmal appearance of the target lesion, larger vessels, lesion calcification, higher patient age, longer lesions and lower balloon pressure [21, 30]. This is in line with the above statement that acute SM is most likely technique dependent, since these predictors are contributing to the complexity of the target lesion or to the technique itself.

Also for late SM, several factors related to the different proposed mechanisms of SM have been shown to be independent predictors.

The highest incidence of 25% of late SM in DES stented patients has been reported in the MISSION! Intervention study, including patients with acute myocardial infarction [21]. Several studies have shown AMI as an independent predictor of SM [14, 16]. The explanation for this can be found in the second proposed mechanism of SM, since the presence of a thrombus, particularly large thrombus load, which is frequently encountered in AMI may predispose to the occurrence of SM later after the dissolution of the thrombus at the site of stent implantation.

Diabetes mellitus has been associated with a lower rate of stent malapposition. The diabetic subpopulation is known to have an increased neointimal growth leading to more restenosis in BMS. Poor glycemic control has been associated with diminished efficacy of sirolimus on smooth muscle cell proliferation, which may explain the lower rate of late SM in these patients [21, 30-32]. Opposing these reports however, another study found a significant greater proportion of diabetic patients in DES cohort with late SM compared to the BMS cohort [14]. They reasoned that the proinflammatory role of diabetes may be responsible for a local enhanced inflammatory reaction after DES implantation eventually increasing the risk of late SM.

Another predictor of SM is directional coronary atherectomy (DCA) before stenting. The higher incidence of late SM in DCA before stenting might be explained by the fact that aggressive debulking with DCA is associated with deep vessel injury and promotes more positive remodeling [15].

Despite angiographic optimization with high pressures and adequately sized balloons, malapposed stent struts are frequently found in complex coronary lesions and more often following the implantation of Cypher Select stents which have a thicker stent strut and closed cell design [33]. Other factors associated with the lesion complexity, such as longer stent length, C-type lesions and overlapping stents, larger vessel reference diameter, have also been associated with an increased risk of SM [14, 16, 21]. Also, chronic total occlusion (CTO), defined by the absence of antegrade flow or only minimal flow of contrast distal to the occlusion during coronary angiography before stent implantation, has been reported as an independent predictor of late SM after DES implantation [16].

Patient age has been associated with the risk of SM, although not consistently. In a recent report of Steinberg et al., subjects with acute SM are older than those without acute SM, whereas (younger) age was the only independent predictor of late acquired SM. Their explanation for this last finding is that most of the other reported risk factors for SM were excluded from their study [30].

As will be discussed in the next section, also the stent type is associated with the risk of late stent malapposition. All risk factors are summarized in Table 1.

Table 1. Risk factors for stent malapposition

Clinical factors	Procedure related factors
Acute myocardial infarction (L)	Drug eluting stent (L)
Absence of diabetes mellitus (L)	Lower maximum balloon pressure (A, L)
Chronic total occlusion (L)	Larger vessel reference diameter (A, L)
Patient age (A,L)	Longer stent length (A, L)
	Overlapping stents (A, L)
	C-type lesion (A,L)
	Directional coronary artherectomy (L)

(A) Risk factor for acute stent malapposition, (L) Risk factor for late stent malapposition

BMS VERSUS DES

Acute SM is frequently observed both after DES and BMS implantation [21, 30]. Considering the mechanism of acute SM, a similar incidence in both DES and BMS is in the line of expectation. Late SM is rare after BMS and seems to be related to stent under-expansion in most patients [21]. Although not all, several studies have reported that late SM is much more common after DES implantation [6, 14, 21, 24, 30, 34]. A recent meta-analysis of Hassan et al, aimed on clarifying this, included 2453 patient after BMS implantation and 2195 patients receiving DES from a total of 17 studies [20]. The incidence of late acquired SM after DES varied between 0% and 25%, whereas after BMS implantation the highest reported incidence of SM was 6% at 6 months. They concluded that the risk of late acquired SM was 4.4-fold higher in patients after DES implantation compared to those with BMS. A comparison of paclitaxel- with –limus-eluting stents did not yield significant findings. The higher risk of SM after DES is likely due to the effects of the drugs on the vessel wall, resulting in positive remodeling [20, 21] In BMS the lumen changes at the site of SM are more related to plaque burden [21].

Furthermore, Hassan et al. also conducted a meta-analysis on the risk of (very) late stent thrombosis in patients with late SM. They concluded that the risk of stent thrombosis is 6.5 times higher (95% confidence interval 1.34-34.91) in patients with late SM compared with those without late SM [20].

So late SM appears to be more frequent after DES implantation and is associated with an increased risk of late stent thrombosis. After adequately lowering the incidence of restenosis, the primary complication of balloon dilatation and BMS implantation, we may have created a potentially more devastating obstacle with late SM and subsequent stent thrombosis in DES.

DIAGNOSTICS

Although intravascular ultrasound (IVUS) has been usually regarded as the gold standard for in vivo assessment of stent strut apposition to the vessel wall, more accurate evaluation of stent strut apposition cannot be successfully performed in some lesions with minimal stent malapposition due to the limited resolution capacity in IVUS (100-150um) [35]. Furthermore, this limited axial resolution of IVUS makes it virtually impossible to discriminate between atherosclerotic plaque and thrombus [21]. It also has problems with stent-related artifacts [12], possibly resulting in underestimation of the evaluation of re-endothelialization. SM is associated with a decreased re-endothelialization after DES implantation [22], which is in turn associated with an increased risk of stent thrombosis [7].

Optical coherence tomography (OCT) is a relatively new imaging modality. In contrast with IVUS, OCT visualizes intra-coronary features using near-infrared light instead of ultrasound, leading to a far better axial resolution, able to resolve detail up to 10 μm [12]. Multiple studies investigating stent malapposition using OCT and comparing it with IVUS findings have already been published. There is evidence that minimal stent malapposition which is not detectable by IVUS may disappear or decrease in follow-up OCT evaluation [35] and SM without complete re-endothelialization is associated with presence of OCT-detected thrombus [12]. More detailed information provided by OCT imaging also led to the conclusion that rate of stent strut coverage and malapposition were significantly different among different DES types and among the type of clinical presentation. More SM was found in sirolimus-eluting stents and paclitaxel-eluting stents compared to zotarolimus-eluting stents and the rate of SM was higher in patients presenting with acute coronary syndrome compared to those with stable angina pectoris [36, 37]. Despite the clear advantages of OCT over IVUS, some disadvantages should also be mentioned. The cost of the device is higher than that of IVUS and the device is not available in every center. A major limitation of OCT is the requirement of a blood-free imaging field because red blood cells scatter light. This can be achieved with a continuous saline flush administration or with a temporary balloon occlusion catheter, leading to transient ischaemia which is not desirable and or tolerated in all cases. Another disadvantage of OCT is poor penetration into non-transparent tissues thus allowing evaluation of only superficial structures including coronary plaques with thin-caps [38].

TREATMENT

The most important and potential devastating complication of SM is stent thrombosis. The mechanism by which SM may contribute to stent thrombosis remains unclear. SM may serve as a local nidus for thrombus formation, allowing fibrin and platelet deposition. Delayed re-endothelialization, impaired vasomotion and also involvement of chronic inflammation

and delayed healing, leading to tissue necrosis around the stent, all contribute to creating a thrombogenic environment [20, 23].
When performing intravascular imaging directly post stent implantation, immediate action can be taken after diagnosing acute stent malapposition by re-dilatation of the target lesion, further expanding the stent. Considering dissolution of a jailed thrombus as a possible mechanism of SM, it may be important to effectively remove thrombotic material prior to stent implantation. Unfortunately, it has been shown that immediate post-intervention IVUS showing no malapposition does not guarantee an uneventful course after DES implantation [8].
After diagnosing stent malapposition during follow-up, defining a proper treatment strategy is difficult, especially when the patient is asymptomatic. The main goal should be off course to prevent stent thrombosis. One option could be pharmacological with long-term double anti-thrombotic treatment [11]. However, this will also lead to a continuous increased bleeding risk and it is evident that SM may also persist for years without leading to complications, creating a risk of exposing patients to unnecessary side effects of the treatment without having the benefit of it. Another option could be dilatation and implantation of a second, larger, stent [39].

FUTURE PERSPECTIVES

It goes without saying that all the, until now, unanswered questions about the mechanism of stent malapposition, its association with stent thrombosis and the best treatment of SM are to be clarified in future larger studies.

One of the current developments in this field is the development of a bioabsorbable stent. The theoretical advantages of such a stent is that it might have less potential for late stent thrombosis because there will eventually be no foreign material exposed to the bloodstream.
Also problems with later surgical revascularization, eliminating vasomotor reactions and interference with imaging techniques could be prevented [40]. However, this remains to be proven and also partial/unequal stent dissolution may perhaps cause problems.

Lately, there have been some ongoing clinical trials addressing the use of self-expandable nitinol stents in the treatment of AMI patients with long-term follow-up IVUS and OCT [41-43]. The hypothesis generated in these trials was that the self-expandable stents would better accommodate to early changes in the vessel wall (thrombus dissolution and vasodilatation) with better apposition due to its self-expandable properties. Initial results have shown that these stents provided 20% increase in lumen area with perfect apposition on 3 days follow up OCT. However, long-term (safety) results are still lacking.

CONCLUSION

Stent malapposition appears to be a relative common finding after stent implantation, especially diagnosed using OCT which has a superior resolution compared to IVUS. The incidence of late SM is higher after DES implantation, mainly caused by positive vascular remodeling. Although SM is associated with stent thrombosis, this is a relatively rare complication. Since the incidence of SM is vastly greater than that of stent thrombosis, SM is not necessarily sine qua non, but more likely only one factor in a complex system. Nevertheless, stent thrombosis is a devastating complication and must be prevented where possible. Therefore, further research unraveling the exact mechanisms of stent malapposition and stent thrombosis and possible treatments will continue in future clinical trials.

REFERENCES

1. Iakovou I, Schmidt T, Bonizzoni E et al. *Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents.* JAMA 2005 May 4;293(17):2126-30.
2. Jeremias A, Sylvia B, Bridges J et al. *Stent thrombosis after successful sirolimus-eluting stent implantation*. Circulation 2004 April 27;109(16):1930-2.
3. McFadden EP, Stabile E, Regar E et al. *Late thrombosis in drug-eluting coronary stents after discontinuation of antiplatelet therapy*. Lancet 2004 October 23;364(9444):1519-21.
4. Cook S, Wenaweser P, Togni M et al. *Incomplete stent apposition and very late stent thrombosis after drug-eluting stent implantation.* Circulation 2007 May 8;115(18):2426-34.
5. Cook S, Ladich E, Nakazawa G et al. *Correlation of intravascular ultrasound findings with histopathological analysis of thrombus aspirates in patients with very late drug-eluting stent thrombosis*. Circulation 2009 August 4;120(5):391-9.
6. Lee CW, Kang SJ, Park DW et al. *Intravascular ultrasound findings in patients with very late stent thrombosis after either drug-eluting or bare-metal stent implantation*. J Am Coll Cardiol 2010 May 4;55(18):1936-42.
7. Luscher TF, Steffel J, Eberli FR et al. *Drug-eluting stent and coronary thrombosis: biological mechanisms and clinical implications*. Circulation 2007 February 27;115(8):1051-8.
8. Bergheanu SC, Van der Hoeven BL, Hassan AK et al. *Post-intervention IVUS is not predictive for very late in-stent thrombosis in drug-eluting stents*. Acta Cardiol 2009 October;64(5):611-6.
9. Alfonso F, Suarez A, Angiolillo DJ et al. *Findings of intravascular ultrasound during acute stent thrombosis*. Heart 2004 December;90(12):1455-9.
10. Alfonso F, Suarez A, Perez-Vizcayno MJ et al. *Intravascular ultrasound findings during episodes of drug-eluting stent thrombosis*. J Am Coll Cardiol 2007 November 20;50(21):2095-7.
11. Alfonso F, Cruz A, Garcia J. *Late stent malapposition: innocent phenomenon or major risk marker?* Eur Heart J 2010 January;31(2):260-1.
12. Ozaki Y, Okumura M, Ismail TF et al. *The fate of incomplete stent apposition with drug-eluting stents: an optical coherence tomography-based natural history study*. Eur Heart J 2010 June;31(12):1470-6.
13. Hur SH, Ako J, Honda Y, Sudhir K, Fitzgerald PJ. *Late-acquired incomplete stent apposition: morphologic characterization*. Cardiovasc Revasc Med 2009 October;10(4):236-46.
14. Chechi T, Vecchio S, Lilli A et al. *Mechanisms of late stent malapposition after primary stenting in ST-elevation myocardial infarction: a subanalysis of the selection trial*. J Interv Cardiol 2009 June;22(3):201-6.
15. Hong MK, Mintz GS, Lee CW et al. *Incidence, mechanism, predictors, and long-term prognosis of late stent malapposition after bare-metal stent implantation*. Circulation 2004 February 24;109(7):881-6.
16. Hong MK, Mintz GS, Lee CW et al. *Late stent malapposition after drug-eluting stent implantation: an intravascular ultrasound analysis with long-term follow-up*. Circulation 2006 January 24;113(3):414-9.
17. Mintz GS, Shah VM, Weissman NJ. *Regional remodeling as the cause of late stent malapposition*. Circulation 2003 June 3;107(21):2660-3.
18. Shah VM, Mintz GS, Apple S, Weissman NJ. *Background incidence of late malapposition after bare-metal stent implantation.* Circulation 2002 October 1;106(14):1753-5.
19. Kang SJ, Mintz GS, Park DW et al. *Late and Very Late Drug-Eluting Stent Malapposition: Serial 2-Year Quantitative IVUS Analysis.* Circ Cardiovasc Interv 2010 July 6.
20. Hassan AK, Bergheanu SC, Stijnen T et al. *Late stent malapposition risk is higher after drug-eluting stent compared with bare-metal stent implantation and associates with late stent thrombosis*. Eur Heart J 2010 May;31(10):1172-80.
21. Van der Hoeven BL, Liem SS, Dijkstra J et al. *Stent malapposition after sirolimus-eluting and bare-metal stent implantation in patients with ST-segment elevation myocardial infarction: acute and 9-month intravascular ultrasound results of the MISSION! intervention study*. JACC Cardiovasc Interv 2008 April;1(2):192-201.
22. Finn AV, Nakazawa G, Joner M et al. *Vascular responses to drug eluting stents: importance of delayed healing.* Arterioscler Thromb Vasc Biol 2007 July;27(7):1500-10.

23. Shiran A, Weissman NJ, Leiboff B et al. *Effect of preintervention plaque burden on subsequent intimal hyperplasia in stented coronary artery lesions*. Am J Cardiol 2000 December 15;86(12):1318-21.
24. Ako J, Morino Y, Honda Y et al. *Late incomplete stent apposition after sirolimus-eluting stent implantation: a serial intravascular ultrasound analysis.* J Am Coll Cardiol 2005 September 20;46(6):1002-5.
25. Costa MA, Sabate M, Kay IP et al. *Three-dimensional intravascular ultrasonic volumetric quantification of stent recoil and neointimal formation of two new generation tubular stents*. Am J Cardiol 2000 January 15;85(2):135-9.
26. Levisay JP, Roth RM, Schatz RA. *Coronary artery aneurysm formation after drug-eluting stent implantation*. Cardiovasc Revasc Med 2008 October;9(4):284-7.
27. van der Giessen WJ, Lincoff AM, Schwartz RS et al. *Marked inflammatory sequelae to implantation of biodegradable and nonbiodegradable polymers in porcine coronary arteries*. Circulation 1996 October 1;94(7):1690-7.
28. Nebeker JR, Virmani R, Bennett CL et al. *Hypersensitivity cases associated with drug-eluting coronary stents: a review of available cases from the Research on Adverse Drug Events and Reports (RADAR) project.* J Am Coll Cardiol 2006 January 3;47(1):175-81.
29. Virmani R, Guagliumi G, Farb A et al. *Localized hypersensitivity and late coronary thrombosis secondary to a sirolimus-eluting stent: should we be cautious?* Circulation 2004 February 17;109(6):701-5.
30. Steinberg DH, Mintz GS, Mandinov L et al. *Long-term impact of routinely detected early and late incomplete stent apposition: an integrated intravascular ultrasound analysis of the TAXUS IV, V, and VI and TAXUS ATLAS workhorse, long lesion, and direct stent studies.* JACC Cardiovasc Interv 2010 May;3(5):486-94.
31. Patterson C, Mapera S, Li HH et al. *Comparative effects of paclitaxel and rapamycin on smooth muscle migration and survival: role of AKT-dependent signaling*. Arterioscler Thromb Vasc Biol 2006 July;26(7):1473-80.
32. Tanabe K, Serruys PW, Degertekin M et al. *Incomplete stent apposition after implantation of paclitaxel-eluting stents or bare metal stents: insights from the randomized TAXUS II trial*. Circulation 2005 February 22;111(7):900-5.
33. Tanigawa J, Barlis P, Dimopoulos K, Dalby M, Moore P, Di MC. *The influence of strut thickness and cell design on immediate apposition of drug-eluting stents assessed by optical coherence tomography*. Int J Cardiol 2009 May 15;134(2):180-8.
34. Jimenez-Quevedo P, Sabate M, Angiolillo DJ et al. *Vascular effects of sirolimus-eluting versus bare-metal stents in diabetic patients: three-dimensional ultrasound results of the Diabetes and Sirolimus-Eluting Stent (DIABETES) Trial*. J Am Coll Cardiol 2006 June 6;47(11):2172-9.
35. Kim WH, Lee BK, Lee S et al. *Serial changes of minimal stent malapposition not detected by intravascular ultrasound: follow-up optical coherence tomography study*. Clin Res Cardiol 2010 April 21.
36. Fan C, Kim JS, Lee JM et al. *Different vascular healing patterns with various drug-eluting stents in primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: optical coherence tomographic findings*. Am J Cardiol 2010 April 1;105(7):972-6.
37. Kim JS, Fan C, Choi D et al. *Different patterns of neointimal coverage between acute coronary syndrome and stable angina after various types of drug-eluting stents implantation; 9-month follow-up optical coherence tomography study*. Int J Cardiol 2009 August 24.
38. Low AF, Tearney GJ, Bouma BE, Jang IK. *Technology Insight: optical coherence tomography--current status and future development.* Nat Clin Pract Cardiovasc Med 2006 March;3(3):154-62.
39. Roura G, Teruel LM, Gomez-Hospital JA. *Very late stent thrombosis due to late stent malapposition*. Rev Esp Cardiol 2009 December;62(12):1499-501.
40. Serruys PW, Ormiston JA, Onuma Y et al. A *bioabsorbable everolimus-eluting coronary stent system (ABSORB): 2-year outcomes and results from multiple imaging methods*. Lancet 2009 March 14;373(9667):897-910.
41. IJsselmuiden A, Verheye S. *First report on the use of a novel self-expandable stent for treatment of ST elevation myocardial infarction.* Catheter Cardiovasc Interv 2009 November 15;74(6):850-4.
42. Verheye S. *Latest results of the STENTYS clinical program.* 2010. Oral presentation Euro PCR congress 2010.
43. Koolen J. STENTYS - *Innovation in Self-Expanding Stent Technology.* 2010. Oral presentation Euro PCR congress 2010.