

관상동맥 스텐트 시술 후 신생내막형성에 관여하는 예측인자 : 혈관내 초음파 연구

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Intravascular Ultrasonic Predictors of Intimal Hyperplasia after Coronary Stenting

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ABSTRACT

Background : Several studies using intravascular ultrasound (IVUS) have suggested several factors to predict for the prediction of angiographic restenosis or intimal hyperplasia (IH) after stenting. However, independent factors to predict IH have not been reported. Therefore, we evaluated the independent predictors of IH after stenting. **Methods** : The serial Serial (pre- and post-intervention, and follow-up) IVUS images were obtained in 77 patients with single stent implantation (GFX in 46 patients and NIR in 31). The matching IVUS image slices at from 4 different sites within the same stent (follow-up lesion site, center of the stent and within 2 mm of the proximal and distal margin of the stent) were selected for serial comparisons. Total A total of 308 matching images were obtained. A number of pre- and post-intervention IVUS variables including remodeling index = (lesion/proximal reference segment) pre-intervention vessel area were entered into a multivariate linear regression analysis model to predict the percent IH. **Results** : The independent IVUS predictors of percent IH were pre-intervention plaque burden at the follow-up lesion site ($r = 0.252$, $p = 0.027$) and the proximal margin of the stent ($r = 0.245$, $p = 0.034$), and pre-intervention plaque burden ($r = 0.334$, $p = 0.003$) and remodeling index ($r = -0.353$, $p = 0.002$) at the center of the stent, and remodeling index at the distal margin of the stent ($r = -0.230$, $p = 0.046$). The percent IH was positively correlated with pre-intervention plaque burden and inversely with remodeling index. **Conclusions** : The independent IVUS predictors of a greater percent IH are larger pre-intervention plaque burden and smaller remodeling index. Ed., Perhaps I am wrong here, but "percent IH" does not seem grammatically correct. It would be better rendered as "the percentage value of the IH". However, if "percent IH" is a convention, i.e. it is used in your field in this manner, then go ahead and use it. If not, and you choose to accept my suggestion, make the changes all the way through. (Korean Circulation J 2001;31(2):191-199)

KEY WORDS : Stent · Restenosis · Intravascular ultrasound.

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서론

35

90

28, 77, 77

가 (Intravascular 50% ultrasound, IVUS) 46 GFX stent(length 12 24 mm, Arterial Vascular Engineering, Inc.)가 hyperplasia, IH) ¹⁾²⁾ 31 NIR stent (quantitative coronary angiographic analysis, QCA) (length 16 25 mm, Boston Scientific Corporation)

가 ³⁻⁸⁾ 스텐트 시술 방법 plaque burden, ⁹⁻¹¹⁾ (electively) (angiographic in - stent restenosis) atheroablation ³⁾⁴⁾ act - plaque burden ivated clotting time 300 ⁵⁻⁷⁾ heparin modeling pattern : (re - (stent optimization) IVUS or negative remodeling)⁸⁾ , positive 가 {minimum lumen cross - sectional (intimal area(CSA) 80% of average of proximal and distal reference lumen CSA or a minimum stent CSA 7.5 mm²) 가 (apposi - tion) aspirin (200 mg/d) ticlopidine(250 mg bid for 1 month) cilostazol(100 mg bid for 1 month)

(IVUS pre - 혈관 내 초음파 시술 방법 dictor)

대상 및 방법

0.2 mg

10 mm

motor - drive pull back system

대 상 140 non - ostial de novo 가 0.5 mm 122 1/2 inch S - VHS 63 strut flexible shaft 3.2 F short

monorail imaging sheath 1,800 rpm
30 MHz single element beveled transducer
system(Boston Scientific Corporation/Cardiovascular Imaging System, Inc.)

정량적 관상동맥 조영술의 분석(Quantitative coronary angiographic analysis, QCA)

0.2 mg

가 online
QCA system(ANCOR V2.0, Siemens),
(minimal luminal diameter),
(reference vessel luminal diameter)

가 50%

정량적 혈관 내 초음파 분석(Quantitative IVUS measurements)

external elastic membrane(EEM), lumen plaque & media(P+M)
(cross-sectional area, CSA)

¹²⁾¹³⁾ EEM CSA

(adventitia) tracing

Plaque & media(P+M) EEM CSA

lumen CSA P+M CSA

EEM CSA plaque burden

(target lesion)

(pre-intervention

lesion site)

가 plaque burden(largest P+M CSA)

5 mm 가

computerized

planimetry EEM,

matching IVUS

4 (,
2 mm)

; (1) pre-intervention plaque

burden(%) = 100(P+M CSA/EEM CSA) pre-intervention,

(2) remodeling index = (lesion/proximal reference segment) pre-intervention EEM CSA,

(3) vessel stretching(mm²) = (post-intervention pre-intervention) EEM CSA, (4) percent vessel

stretching(%) = 100(post-intervention EEM CSA pre-intervention EEM CSA)/pre-intervention EEM

CSA, (5) persistent P+M CSA(mm²) = (EEM CSA - stent CSA) post-intervention, (6) residual plaque

burden(%) = 100(persistent P+M CSA/EEM CSA) post-intervention, (7) IH CSA(mm²) = (stent CSA

lumen CSA) follow-up (8) percent IH CSA (%) = 100(IH CSA/stent CSA) follow-up(Fig. 1).

Reproducibility of IVUS measurements

가 EEM 가
strut
10 2 가 EEM,

통계분석

SPSS program(version 8.0)

unpaired

t-test, Chi-square Fisher's exact test

linear regression analysis

p-value가 0.2

p-value 0.05

결 과

77 QCA

IVUS data Table 1, 2 and 3

6.5 ± 1.7 . =0.922 in lumen CSA at follow - up.
 GFX 11 NIR (univariate analysis)
 5 (Table 4 percent IH
 1, 2 and 3). (follow - up lesion site in Table
 (diffuse in - stent restenosis) 8 , 4, distal margin in Table 5, center of the stent in
 (focal in - stent restenosis) 8 (proximal part Table 6 proximal margin in Table 7).
 2 , center 3 distal part 3) p - value가 0.2
 Reproducibility study ; r
 =0.914 in EEM CSA and r=0.955 in stent CSA at percent IH
 post - intervention, and r=0.943 in stent CSA and r pre -

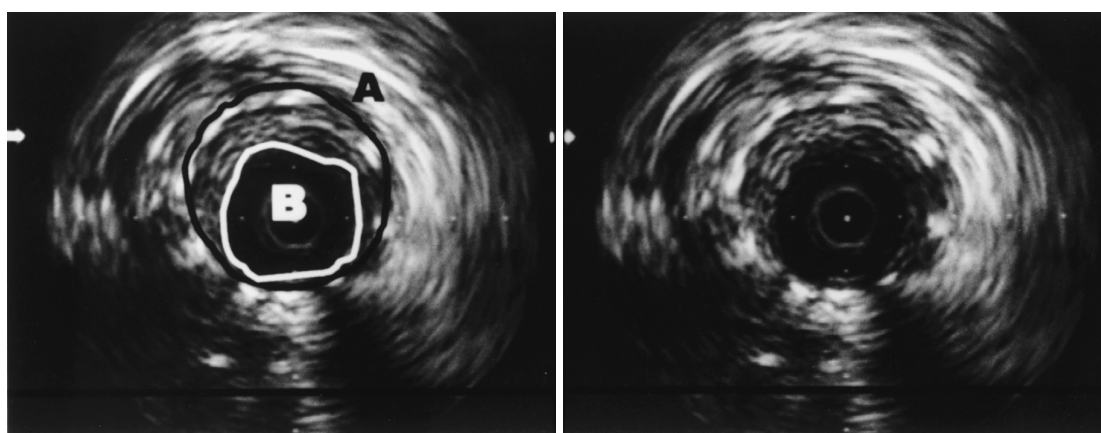


Fig. 1. This figure shows the methods to calculate intimal hyperplasia (IH) cross-sectional area (CSA) and percent IH CSA. Left and right follow-up intravascular ultrasound images are identical. A and B represents stent CSA and lumen CSA at follow-up, respectively. IH CSA (mm²) : A - B, Percent IH CSA (%) : 100 × (A - B)/A.

Table 1. Baseline clinical characteristics (%)

	Total	No restenosis	Restenosis	p
Number of patients	77	61	16	
Age (years)	58 ± 9	57 ± 8	60 ± 10	0.287
Males	66 (86)	52 (85)	14 (88)	0.590
Prior myocardial infarction	8 (10)	7 (11)	1 (6)	0.472
Hypertension	25 (33)	20 (33)	5 (31)	0.580
Diabetes mellitus	9 (12)	7 (12)	2 (13)	0.600
Hypercholesterolemia	9 (12)	7 (12)	2 (13)	0.600
Cigarette smoking	45 (58)	35 (57)	10 (63)	0.470
Clinical presentation				0.769
Stable angina	20 (26)	16 (26)	4 (25)	
Unstable angina	43 (56)	33 (54)	10 (63)	
Acute myocardial infarction	14 (18)	12 (20)	2 (13)	
Number of disease vessel				0.985
One	54 (70)	43 (71)	11 (69)	
Two	18 (23)	14 (23)	4 (35)	
Three	5 (7)	4 (6)	1 (6)	

intervention plaque burden($r=0.252$, $p=0.027$ at follow - up lesion site, Fig. 2 and $r=0.245$, $p=0.034$ at proximal margin of stent, Fig. 3), pre - intervention plaque burden($r=0.334$, $p=0.003$) remodeling index($r=-0.353$, $p=0.002$)(Fig. 4), remodeling index($r=-0.230$, $p=0.046$) (Fig. 5). Percent IH plaque burden (pre - intervention plaque burden) , remodeling index . Remodeling index

Table 2. Baseline angiographic characteristics and procedural results(%)

	Total	No restenosis	Restenosis	p
Number of lesions	77	61	16	
Coronary artery dilated				0.477
Left anterior descending	54 (70)	42 (69)	12 (74)	
Left circumflex	6 (8)	4 (6)	2 (14)	
Right coronary	17 (22)	15 (25)	2 (13)	
Stent length (mm)	17.8 ± 4.1	17.9 ± 4.1	17.6 ± 4.0	0.819
Reference vessel diameter (mm)	3.6 ± 0.5	3.6 ± 0.5	3.4 ± 0.4	0.107
Minimal lumen diameter (mm)				
Pre-intervention	0.9 ± 0.5	0.9 ± 0.5	0.7 ± 0.4	0.692
Post-intervention	3.6 ± 0.5	3.6 ± 0.5	3.4 ± 0.6	0.156
Follow-up	2.1 ± 0.8	2.4 ± 0.6	1.1 ± 0.5	0.000
Balloon-to artery ratio	1.09±0.10	1.10±0.10	1.07±0.08	0.133
Pressure (atm)	12.0 ± 3.5	12.1 ± 3.6	11.8 ± 3.2	0.882

Table 3. Intravascular ultrasound findings

	Total (n = 77)	No restenosis (n = 61)	Restenosis (n = 16)	p
Pre-intervention				
Proximal reference segment				
EEM CSA (mm ²)	16.0± 2.8	15.9± 2.7	16.5± 3.3	0.506
Lumen CSA (mm ²)	8.3± 2.2	8.3± 2.1	8.4± 2.4	0.878
Plaque burden (%)	48± 11	47± 11	49± 10	0.620
Lesion segment				
EEM CSA (mm ²)	15.4± 2.8	15.6± 2.8	14.6± 2.8	0.225
Lumen CSA (mm ²)	2.0± 0.7	2.0± 0.7	1.8± 0.4	0.339
Plaque burden (%)	87± 5	87± 5	88± 3	0.688
Remodeling index	0.97± 0.10	1.00± 0.09	0.89± 0.09	0.001
Post-intervention				
EEM CSA (mm ²)	17.7± 3.3	17.9± 3.2	16.9± 3.7	0.319
Stent CSA (mm ²)	8.9± 2.2	9.0± 2.1	8.3± 2.6	0.329
Residual plaque burden (%)	50± 8	50± 8	51± 8	0.512
Percent vessel stretching (%)	17± 8	16± 8	19± 9	0.171
Follow-up				
Stent CSA (mm ²)	9.5± 2.4	9.7± 2.3	8.6± 2.8	0.166
Lumen CSA (mm ²)	4.7± 2.1	5.5± 1.5	1.7± 0.5	0.000
IH CSA (mm ²)	4.8± 2.4	4.2± 2.0	7.0± 2.5	0.001
Percent IH CSA (%)	50± 20	42± 14	80± 5	0.000

EEM : external elastic membrane, CSA : cross sectional area, IH : intimal hyperplasia

Table 4. Intravascular ultrasound predictors of intimal hyperplasia by univariate analysis at the follow-up lesion site

	Total (n = 77)	r	p
Pre-intervention			
EEM CSA (mm ²)	15.5 ± 3.1	0.222	0.052
Lumen CSA (mm ²)	4.2 ± 2.1	- 0.117	0.312
Plaque burden (%)	73 ± 12	0.252	0.027
Remodeling index*	0.97 ± 0.11	- 0.148	0.198
Post-intervention			
EEM CSA (mm ²)	18.1 ± 3.3	0.216	0.061
Stent CSA (mm ²)	9.5 ± 2.5	0.099	0.392
Residual plaque burden (%)	48 ± 8	0.135	0.245
Vessel stretching (mm ²)	2.6 ± 1.4	0.031	0.787
Percent vessel stretching (%)	18 ± 10	0.048	0.679

* : Independent predictors in multivariate analysis
EEM : external elastic membrane
CSA : cross sectional area
IH : intimal hyperplasia

Table 5. Intravascular ultrasound predictors of intimal hyperplasia by univariate analysis at the distal margin

	Total (n = 77)	r	p
Pre-intervention			
EEM CSA (mm ²)	15.0 ± 3.1	0.120	0.303
Lumen CSA (mm ²)	6.4 ± 2.5	- 0.125	0.283
Plaque burden (%)	58 ± 12	0.093	0.425
Remodeling index*	0.95 ± 0.11	- 0.230	0.046
Post-intervention			
EEM CSA (mm ²)	17.3 ± 3.3	0.105	0.365
Stent CSA (mm ²)	10.0 ± 2.5	0.093	0.427
Residual plaque burden (%)	43 ± 8	0.068	0.562
Vessel stretching (mm ²)	2.3 ± 1.3	0.018	0.878
Percent vessel stretching (%)	16 ± 10	0.017	0.881

* : Independent predictors in multivariate analysis
EEM : external elastic membrane
CSA : cross sectional area
IH : intimal hyperplasia

(r = - 0.387, p=0.001 at the center of stent, r = - 0.438, p=0.000 and r = - 0.359, p = 0.002 within 2 mm of distal and proximal margin of stent, respectively) percent vessel stretching

Table 6. Intravascular ultrasound predictors of intimal hyperplasia by univariate analysis at the center of the stent

	Total (n = 77)	r	p
Pre-intervention			
EEM CSA (mm ²)	15.5 ± 3.0	0.088	0.445
Lumen CSA (mm ²)	3.8 ± 2.0	- 0.344	0.002
Plaque burden (%)	76 ± 11	0.334	0.003
Remodeling index*	0.97 ± 0.11	- 0.353	0.002
Post-intervention			
EEM CSA (mm ²)	18.3 ± 3.2	0.007	0.953
Stent CSA (mm ²)	9.6 ± 2.3	0.001	0.992
Residual plaque burden (%)	48 ± 7	0.020	0.863
Vessel stretching (mm ²)	2.7 ± 1.6	0.142	0.223
Percent vessel stretching (%)	18 ± 11	0.133	0.254

* : Independent predictors in multivariate analysis
EEM : external elastic membrane
CSA : cross sectional area
IH : intimal hyperplasia

Table 7. Intravascular ultrasound predictors of intimal hyperplasia by univariate analysis at the proximal margin

	Total (n = 77)	r	p
Pre-intervention			
EEM CSA (mm ²)	16.8 ± 3.5	0.020	0.866
Lumen CSA (mm ²)	6.3 ± 2.4	- 0.187	0.105
Plaque burden (%)	63 ± 11	0.245	0.034
Remodeling index*	1.01 ± 0.09	- 0.163	0.161
Post-intervention			
EEM CSA (mm ²)	19.0 ± 3.9	0.081	0.485
Stent CSA (mm ²)	10.3 ± 2.5	0.018	0.877
Residual plaque burden (%)	46 ± 7	0.132	0.252
Vessel stretching (mm ²)	2.2 ± 1.6	0.127	0.278
Percent vessel stretching (%)	14 ± 10	0.094	0.423

* : Independent predictors in multivariate analysis
EEM : external elastic membrane
CSA : cross sectional area
IH : intimal hyperplasia

고찰

Plaque burden

QCA

(가 plaque burden)

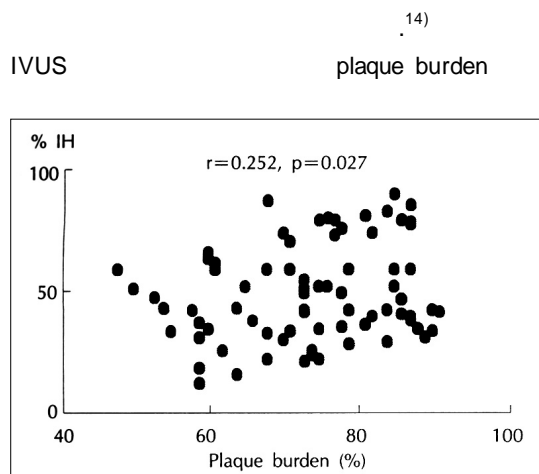


Fig. 2. Pre-intervention plaque burden correlated positively with percent intimal hyperplasia (IH) at the follow-up lesion site ($r=0.252, p=0.027$).

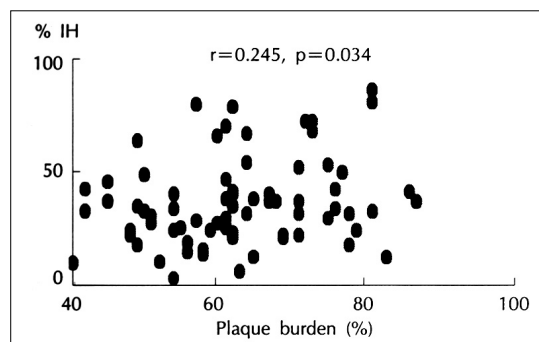


Fig. 3. Pre-intervention plaque burden positively correlated with percent intimal hyperplasia (IH) at the proximal margin of stent ($r=0.245, p=0.034$).

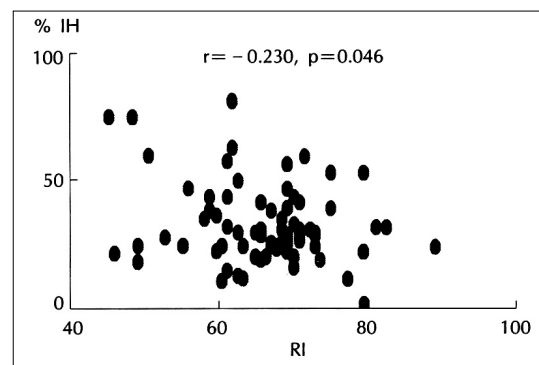
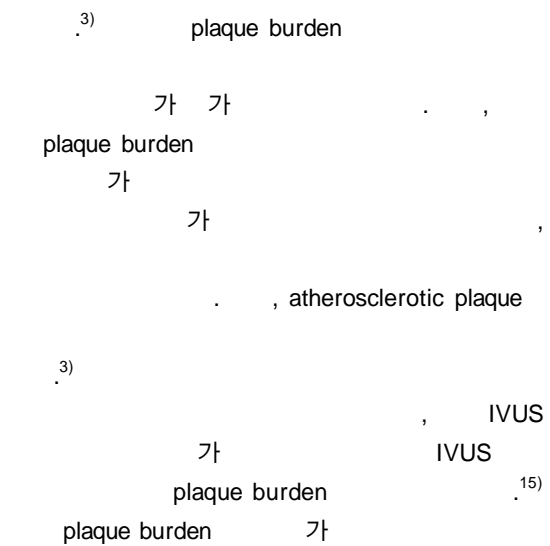
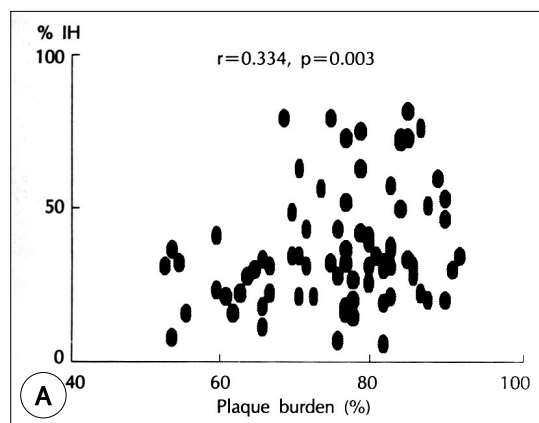


Fig. 5. Remodeling index (RI) inversely correlated with percent intimal hyperplasia (IH) at distal margin of stent ($r=-0.230, p=0.046$).

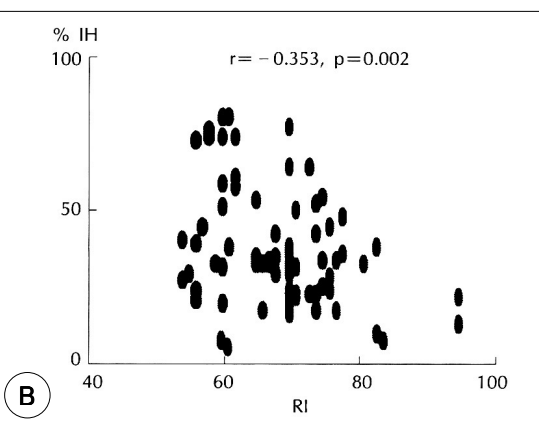


Fig. 4. Pre-intervention plaque burden positively correlated with percent intimal hyperplasia (IH) (A, $r=0.334, p=0.003$) and remodeling index (RI) inversely correlated with percent IH (B, $r=-0.353, p=0.002$) at the center of stent.

(pathologic remodeling) (16%) vs. 14%, p=0.122). plaque burden remodeling index (inadequate remodeling)가 per cent IH CSA

가 plaque burden 연구의 제한점

directional atherectomy debulking EEM

loss index (7)17) 가

3.6 mm, stent CSA 8.9 mm² 가

plaque burden percent IH CSA

요 약

Vascular remodeling and vessel stretching 가

연구목적 :

(positive remodeling)가 QCA late loss (IVUS predictors)

(adequate remodeling) (inadequate remodeling)가 per cent IH CSA

percent vessel stretching remodeling index 가 (=smaller remodeling index)가

방 법 :

77 , 77 (GFX 46 NIR 31)

percent IH(intimal hyperplasia)

결 과 :

remodeling index [= (lesion/proximal reference segment) pre - intervention EEM CSA]

pre - intervention plaque burden (r = 0.252, p = 0.027 at follow - up lesion site and r = 0.245, p = 0.034 at proximal margin of stent)

remodeling index가 (0.95 vs. 1.01, p=0.000),

pre - intervention plaque burden (r = 0.334, p=0.003) remodeling index (r = - 0.353,

p=0.002) ,
remodeling index(r = - 0.230, p=0.046)
. Percent IH plaque burden(pre - in -
tervention plaque burden)
, remodeling index
결 론 :
plaque burden remo -
deling index(inadequate remodeling)가 percent IH
CSA

중심 단어 : . . .

REFERENCES

- Hoffmann R, Mintz GS, Dussaillant GR, Popma JJ, Pichard AP, Satler LF, et al. Patterns and mechanism on in-stent restenosis: A serial intravascular ultrasound study. *Circulation* 1996;94:1247-54.
- Mudra H, Regar E, Klauss V, Werner F, Henneke KH, Sbarouni E, et al. Serial follow-up after optimized ultrasound-guided deployment of Palmaz-Schatz stents. In-stent intimal hyperplasia without significant reference segment response. *Circulation* 1997;95:363-70.
- Hoffmann R, Mintz GS, Mehran R, Pichard AD, Kent KM, Satler LF, et al. Intravascular ultrasound predictors of angiographic restenosis in lesions treated with Palmaz-Schatz stents. *J Am Coll Cardiol* 1998;31:43-9.
- Kasaoka S, Tobis JM, Akiyama T, Reimers B, Di Mario C, Wong ND, et al. Angiographic and intravascular ultrasound predictors of in-stent restenosis. *J Am Coll Cardiol* 1998;32:1630-5.
- Hoffmann R, Mintz GS, Popma JJ, Satler LF, Pichard AD, Kent KM, et al. Chronic arterial responses to stent implantation: A serial intravascular ultrasound analysis of Palmaz-Schatz stents in native coronary arteries. *J Am Coll Cardiol* 1996;28:1134-9.
- Werner F, Regar E, Henneke KH, Johannes R, Andreas K, Metz JA, et al. Vessel stretching is an important factor for neointimal proliferation after stent implantation: An investigation with intravascular ultrasound. *Circulation* 1997;96:1-583.
- Prati F, Di Mario C, Moussa I, Reimers B, Mallus MT, Parma A, et al. In-stent neointimal proliferation correlates with the amount of residual plaque burden outside the stent: An intravascular ultrasound study. *Circulation* 1999;99:1011-4.
- Matsui H, Sakai K, Ajioka M, Asano H. Arterial remodeling before intervention as a possible determinant of restenosis after Palmaz-Schatz stent implantation. *Circulation* 1998;98:1-295.
- Hong MK, Park SW, Mintz GS, Lee NH, Lee CW, Kim JJ, et al. Intravascular ultrasonic predictors of angiographic restenosis after long coronary stenting. *Am J Cardiol* 2000;85:441-5.
- Schomig A, Neumann FJ, Kastrati A, Schuhlen H, Blasini R, Hadamitzky M, et al. A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary artery stents. *N Engl J Med* 1996;334:1084-9.
- Colombo A, Hall P, Nakamura S, Almagor Y, Maiello L, Martini G, et al. Intracoronary stenting without anticoagulation accomplished with intravascular ultrasound guidance. *Circulation* 1995;91:1676-88.
- Tobis JM, Mallery J, Mahon D, Lehmann K, Zalesky P, Griffith J, et al. Intravascular ultrasound imaging of human coronary arteries in vivo: analysis of tissue characteristics with comparison to in vivo histologic specimens. *Circulation* 1991;83:913-26.
- Nishimura RA, Edwards WD, Warnes CA, Reeder GS, Holmes DR, Tajik AJ, et al. Intravascular ultrasound imaging: in vitro validation and pathologic correlation. *J Am Coll Cardiol* 1990;16:145-54.
- Sirnes P, Golf S, Myreng Y, Molstad P, Emanuelsson H, Albertsson P, et al. Stenting in chronic coronary occlusion (SICCO): A randomized, controlled trial of adding stent implantation after successful angioplasty. *J Am Coll Cardiol* 1996;28:1444-51.
- Mintz GS, Popma JJ, Pichard AP, Kent KM, Satler LF, Chuang YC, et al. Intravascular ultrasound predictors of restenosis after percutaneous transcatheter coronary revascularization. *J Am Coll Cardiol* 1996;27:1678-87.
- Mintz GS, Popma JJ, Pichard AP, Kent KM, Satler LF, Wong C, et al. Arterial remodeling after coronary angioplasty: A serial intravascular ultrasound study. *Circulation* 1996;94:35-43.
- Moussa I, Moses J, Di Mario C, Busi G, Reimers B, Kobayashi Y, et al. Stenting after optimal lesion debulking (SOLD) registry: Angiographic and clinical outcomes. *Circulation* 1998;98:1604-9.