Original Research

The Impact of New Generation Drug-Eluting Stent Implantation on Patients with Chronic Kidney Disease and a Single Lesion in the Proximal Segment of the Left Anterior Descending Artery

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Introduction: The impact of drug-eluting stents (DES) has not been extensively investigated in patients with moderate to severe renal dysfunction, as these patients are consistently excluded from randomised studies. We sought to assess prospectively the effectiveness and safety of the new-generation DES in patients with moderate chronic kidney disease (CKD) and an isolated *de novo* lesion in the proximal segment of the left anterior descending artery (pLAD).

Methods: We evaluated 400 consecutive patients with a pLAD lesion. There were 96 patients with moderate CKD (estimated glomerular filtration rate ≤59 ml/min/1.73 m^2) and 304 without CKD. Major adverse cardiac events (MACE) were defined as death, non-fatal myocardial infarction and target lesion revascularisation (TLR). Clinical or telephone follow up was performed.

Results: There was a significantly higher incidence of mortality in patients with CKD (n=4) as compared with non-CKD (n=2) (4.16% versus 0.65%, respectively, p=0.03). The rate of non-fatal myocardial infarction was similar in the 2 cohorts (p=0.59), as was the TLR rate (p=0.99). Overall, there were no significant differences regarding MACE between the 2 groups of patients (p=0.19) during the 13.62 ± 6.22 month follow-up period. The rate of angiographic stent thrombosis was 2.08% in the CKD group versus 0.98% in the non-CKD group (p=0.59).

Conclusions: New generation DES implantation in patients with CKD and a pLAD lesion is effective and safe, with rates of TLR and stent thrombosis comparable to those in patients with normal renal function. However, the higher mortality in patients with CKD needs further evaluation.

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Lesions in the proximal segment of the left anterior descending artery (pLAD) present great clinical interest regarding treatment approach, as this particular anatomical location of the atherosclerotic plaque is associated with increased mortality.[1,2] The use of drug-eluting stents (DES) has improved the clinical and angiographic outcome compared to bare-metal stents. Sirolimus- and paclitaxel- eluting stents, the most extensively studied DES with long-term results, have demonstrated favourable outcomes in patients with a pLAD lesion.[3-7] Similarly, the new-generation DES, zotarolimus- and everolimus-eluting stents, have been shown to be effective and safe in patients with coronary artery disease undergoing percutaneous coronary intervention.[8-13]

The existence of comorbidities such as renal dysfunction in patients with cardiovascular disease is associated with in-

creased mortality and morbidity as compared with patients with normal renal function.[14-16] Furthermore, patients with renal dysfunction who undergo percutaneous coronary intervention with balloon angioplasty or bare-metal stent implantation have an increased mortality rate (up to 46.6%) during the follow-up period, probably due to the coexistence of more cardiovascular risk factors that increase the rate of death and other cardiovascular events. In addition, renal impairment seems to be an independent predictor for an increased mortality rate.[17-25] Therefore, apart from the location and the severity of coronary artery lesions, the presence of renal impairment in patients with coronary artery disease constitutes an independent variable predicting the short- and long-term results after percutaneous coronary intervention.[22] In the DES era, limited data exist regarding their effectiveness and safety in patients with moderate to severe renal dysfunction, as these patients are often excluded from large, randomised trials.[26-33] In this limited number of studies, first-generation DES have shown a higher mortality rate in patients with renal failure, mainly due to the coexistence of comorbidities.

The aim of the present study was to evaluate prospectively the effectiveness and safety of new-generation DES in patients with moderate chronic kidney disease (CKD) and an isolated *de novo* lesion in the pLAD.

Methods

Study population

The study population consisted of 400 consecutive patients who were treated in our cardiovascular department from June 2006 to July 2008. Of these, 96 patients had moderate to severe CKD, defined as an estimated glomerular filtration rate (eGFR) ≤59 ml/min/1.73 m^2, and were not on dialysis, while the remaining 304 patients had normal renal function (non-CKD group). The patients in our study population had an isolated significant (>75%) *de novo* pLAD lesion extending from the ostium to the first diagonal branch. The clinical symptomatology was chronic stable angina or stress-induced ischaemia. Patients with left main and multivessel disease, low ejection fraction (EF <30%), acute coronary syndromes or myocardial infarction during the month prior to intervention, and contraindications for long-term administration of dual antiplatelet therapy were excluded from our study. Patients with comorbidities such as cancer (receiving chemotherapy or radiotherapy), or with immunological diseases were also excluded from the study. Clinical follow up was performed in all patients by interview in our department or by telephone. All patients were scheduled to undergo myocardial scintigraphy at 6 months after DES implantation. Written informed consent was obtained from every patient. Our study protocol was approved by the Hospital Ethics Committee.

Angiographic analysis

Lesions were characterised according to the modified American College of Cardiology/American Heart Association classification. To specify the grade of stenosis as a percentage, we compared the critical portion of stenosis with the lumen of the normal vessel, both proximal and distal to the stenosis area, as a reference. Restenosis was defined as stenosis of more than 50% of the luminal diameter. The angiographic analysis was performed based on coronary angiography for both study groups.

Definitions and endpoints

Restenotic lesions were classified angiographically according to the Mehran classification, as follows:[34] I. *focal* (<10 mm); II. *diffuse* (>10 mm without extending outside the margins of the stent); III. *proliferative* (>10 mm extending the margins of the stent); IV. *total occlusion*.

The incidence of thrombotic events was assessed as total coronary artery occlusion indicated by abrupt onset of symptoms, elevated biochemical markers and electrocardiographic changes consistent with a myocardial infarction. Stent thrombosis was classified according to the Academic Research Consortium (ARC) and was defined as *definite* (angiographic or pathological confirmation of stent thrombosis), *probable* (any unexplained death within 30 days after the procedure, or myocardial infarction related to documented acute ischaemia in the territory of the implanted stent, without angiographic confirmation of stent thrombosis), or *possible* (any unexplained death after 30 days). Stent thrombosis was also classified according to the timing of the occurrence of stent thrombosis: *acute* (within 24 h post implantation), *subacute* (1-30 days), *late* (>30 days to 1 year), and *very late* (>1 year).[35]

The primary endpoint of the study was the inci-

dence of major adverse cardiac events (MACE), including death, non-fatal myocardial infarction and clinically driven target lesion revascularisation (TLR). TLR was defined as any surgical or percutaneous re-intervention at the target lesion. In the case of MACE, the time interval between intervention and occurrence was specified. All deaths that could not be clearly attributed to another cause were considered cardiac deaths. Stent thrombosis events were also recorded.

Percutaneous coronary intervention

All patients were scheduled to receive dual antiplatelet therapy prior to percutaneous coronary intervention with 100 mg of aspirin and a loading dose of 300 mg clopidogrel. Percutaneous coronary intervention was performed using standard techniques and we used zotarolimus-eluting stents (ENDEAVOR, Medtronic, Santa Rosa CA, USA) or everolimus-eluting stents (XIENCE V, Abbott Cardiovascular System, Abbott Vascular Company, CA, USA). The decision whether to implant everolimus-eluting stents or zotarolimus-eluting stents was left to the operator's discretion and was driven by the availability of stent sizes. Femoral or brachial accesses were performed during percutaneous coronary intervention. During the intervention all patients received 70 units/kg bolus IV of unfractionated heparin to maintain an activated partial thromboplastin time at least 2 to 3 times greater than the control value. Predilation of the target lesion and administration of platelet glycoprotein IIb-IIIa inhibitors for 24 hours after the intervention were also left to the operator's discretion. By protocol in our department the target lesion is scheduled to be covered by a single DES. In cases where additional DES were required, the same type of DES was implanted. The combined antiplatelet treatment was scheduled to be administered continuously for at least 12 months after percutaneous coronary intervention, whereas aspirin was prescribed indefinitely.

Evaluation of renal function

The serum creatinine level was measured in all patients before the procedure in our department and was used to calculate the estimated glomerular filtration rate (eGFR) using the Level Modification of Diet in Renal Disease.[36] According to the National Kidney Foundation's Kidney Disease Outcome Quality Initiative Advisory Board, moderate CKD was defined as a calculated eGFR of 30-59 ml/min/1.73m^2.[36]

Statistical analysis

Data for categorical variables are expressed as the number and the percentage of patients. For continuous variables, data are expressed as mean ± SD and were compared using the unpaired Student's t-test. Fisher's exact test or a chi-square test was used for the comparison of categorical variables. Event rates were estimated by the Kaplan-Meier method and compared by means of the log-rank test. A p-value of less than 0.05 was considered significant. All analyses were performed using StatView statistical software (version 5.0).

Results

Patients from the CKD group were older and had a higher rate of hypertension, whereas the non-CKD group patients included a higher percentage of current smokers and males (Table 1). The majority of the lesions were type B1 and B2, 77.08% in the CKD group and 84.86% in the non-CKD group. There were no differences in the procedural characteristics between the two groups, as the total diameter, length, inflation pressure and the number of DES were comparable (Table 2).

Clinical follow up

The rate of death was higher in patients with CKD compared to patients from the non-CKD group: 4 patients (4.16%) versus 2 patients (0.65%), respectively, p=0.03. Specifically, 3 patients from the CKD group suffered sudden death at 6, 12, and 26 months after DES deployment. The fourth patient died from subacute thrombosis 7 days after DES implantation. In the non-CKD group, sudden death occurred at 2 months after DES implantation in one patient and at 8 months in the other. There were no differences in the rates of non-fatal myocardial infarction (p=0.59) or TLR (p=0.99) between the two cohorts. One patient from the CKD group (1.04%) underwent percutaneous coronary intervention 2 years after DES deployment for focal restenosis, and 6 patients (1.97%) from the non-CKD group underwent percutaneous coronary intervention at 7.08 ± 1.08 months after DES implantation because of restenosis, focal in 4 and diffuse in 2. In addition, one patient from the CKD group underwent coronary artery bypass grafting for focal restenosis, while the 3 patients from the non-CKD group underwent surgical revascularisation for restenosis at 7.94 ± 3.14 months. One patient from the latter group

Table 1. Demographic characteristics of the study population.

	CKD (n=96)	Non-CKD (n=304)	p
Age (years)	66.88 ± 10.32	58.96 ± 11.20	0.001
Male gender (%)	65 (67.70%)	261 (85.85%)	0.001
BMI	27.62 ± 3.39	28.39 ± 5.08	0.16
EF (%)	54.2 ± 7.3	53.4 ± 7.3	0.35
Diabetes mellitus (%)	35 (36.45%)	94 (30.92%)	0.31
Oral medication (%)	31 (88.57%)	87 (92.55%)	0.52
Insulin	4 (11.42%)	7 (7.44%)	0.30
Current smokers (%)	27 (28.12%)	152 (50%)	0.002
Previous smokers (%)	26 (27.08%)	82 (26.97%)	0.99
Hypertension (%)	68 (70.83%)	175 (57.56%)	0.02
Under anti-hypertensive treatment (%)	58 (85.29%)	166 (94.85%)	0.34
Family history (%)	31 (32.29%)	113 (37.17%)	0.39
Hypercholesterolaemia (%)	67 (69.79%)	211 (69.40%)	0.99
Under statin medication (%)	55 (82.08%)	152 (72.03%)	0.24
Prior MI >1 month (%)	15 (15.62%)	52 (17.10%)	0.87
Treatment at discharge:			
Aspirin	96 (100%)	304 (100%)	–
Statins	70 (72.91%)	244 (80.26%)	0.15
ACE inhibitors	37 (38.54%)	146 (48.02%)	0.12
Nitrates	45 (46.87%)	136 (44.73%)	0.72
B-blockers	66 (68.75%)	225 (74.01%)	0.35
ARB	25 (26.04%)	75 (24.67%)	0.78
Calcium antagonists	16 (16.66%)	40 (13.15%)	0.40
Clopidogrel	96 (100%)	304 (100%)	–
Serum creatinine (mg/dl)	1.45 ± 0.67	0.98 ± 0.14	0.001
eGFR (ml/min/1.73 m^2)	50.38 ± 9.37	81.51 ± 13.36	0.001

CKD – Chronic kidney disease; BMI – body mass index; EF – ejection fraction; MI – myocardial infarction; ACE – angiotensin converting enzyme; ARB – angiotensin II receptor blockers; eGFR – estimated glomerular filtration rate.

Table 2. Angiographic and procedural characteristics of the study population.

	CKD (n=96)	Non-CKD (n=304)	p
AHA/ACC lesion class:			
A	16 (16.66%)	34 (11.18%)	0.16
B1	36 (37.50%)	135 (44.40%)	0.23
B2	38 (39.58%)	123 (40.46%)	0.90
C	6 (6.25%)	12 (3.94%)	0.39
Procedural characteristics:			
Mean number of stents	1.26 ± 0.63	1.24 ± 0.54	0.83
Mean stent diameter (mm)	2.92 ± 0.32	2.96 ± 0.34	0.27
Mean stent length (mm)	18.53 ± 4.26	19.04 ± 4.44	0.32
Mean inflation pressure (atm)	15.14 ± 1.64	15.30 ± 1.48	0.37
Everolimus-eluting stent	59 (61.45%)	203 (66.77%)	0.38
Zotarolimus-eluting stent	37 (38.54%)	101 (33.22%)	0.38

AHA – American Heart Association; ACC – American College of Cardiology; CKD – chronic kidney disease.

had a total occlusion and the other 2 had focal restenosis. The incidence of angiographic stent thrombosis was 2.08% in the CKD group versus 0.98% in the non-CKD group (p=0.59). Subacute thrombosis was observed in 1 patient (1.04%) from the CKD group and in 2 patients (0.65%) from the non-CKD group, while 1 patient from each group experienced late thrombosis. Of these, only 1 patient from the CKD group had stopped the dual antiplatelet therapy 4 months after DES implantation. The remaining 4 patients were under combined antiplatelet therapy when they experienced angiographically documented thrombosis. The incidence of definite/probable/possible stent thrombosis according to the ARC definition did not differ sta-

Table 3. Stent thrombosis.

	CKD (n=96)	Non-CKD (n=304)	p
Acute	0 (0.0%)	0 (0.0%)	–
Subacute	1 (1.04%)	2 (0.65%)	0.56
Late	1 (1.04%)	1 (0.32%)	0.42
Very late	0 (0.0%)	0 (0.0%)	–
Definite	2 (2.08%)	3 (0.98%)	0.59
Total (definite/probable/possible)	6 (6.25%)	8 (2.63%)	0.11

CKD – chronic kidney disease.

tistically between the 2 groups, although there was a higher rate of total thrombotic events in patients with CKD (6.25% in CKD group vs. 2.63%, p=0.11; Table 3). Overall, there was a higher incidence of MACE in the CKD group, although a statistically significant difference was not found (8.33% vs. 4.60%, p=0.19) during the 13.62 ± 6.22 month follow-up period (Table 4). Finally, the event-free survival curve was similar in both groups: 91.66% in the CKD group vs. 95.39% in the non-CKD group (p=0.21) (Figure 1).

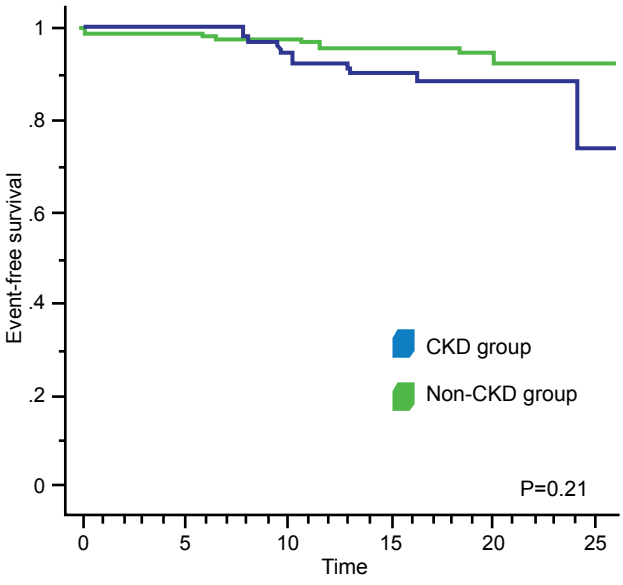

Figure 1. Kaplan-Meier survival curve. Freedom from major adverse cardiac events (MACE) in patients with and without chronic kidney disease (CKD). There is no statistical difference between the 2 groups of patients (p=0.21).

Discussion

The main finding of this study was that patients with moderate CKD and an isolated *de novo* pLAD lesion, suffering from chronic stable angina, who underwent percutaneous coronary intervention with new-generation DES implantation, demonstrated a higher mortality rate during a mid-term follow-up period. In addition, new generation DES demonstrated their effectiveness and safety in patients with CKD, as the TLR and thrombosis rate were comparable with the non-CKD group.

It has repeatedly been documented that the presence of renal impairment in patients who undergo percutaneous coronary intervention with balloon angioplasty or stenting is strongly associated with adverse outcomes regarding the survival rate.[17-25] Similarly, until recently, the mortality rate in patients with renal failure who undergo percutaneous coronary intervention with DES deployment does not seem to improve, according to prior reports.[26-33] Specifically, the rate of death in our study was 4.16% in patients with CKD, which was lower than the mortality reported in previous studies (7.6-29.2%). This difference may be partly explained by the fact that previous studies included patients with left main and multivessel coronary artery disease, saphenous vein graft

Table 4. Clinical outcomes during follow-up period.

	CKD (n=96)	Non-CKD (n=304)	p
Death	4 (4.16%)	2 (0.65%)	0.03
Cardiac	4 (4.16%)	2 (0.65%)	0.03
Non-fatal MI	2 (2.08%)	3 (0.98%)	0.59
TLR	2 (2.08%)	9 (2.96%)	0.99
PCI	1 (1.04%)	6 (1.97%)	0.99
CABG	1 (1.04%)	3 (0.98%)	0.99
MACE	8 (8.33%)	14 (4.60%)	0.19

CKD – chronic kidney disease; MI – myocardial infarction; TLR – target lesion revascularisation; PCI – percutaneous coronary intervention; CABG – coronary artery bypass grafting; MACE – major adverse cardiac events.

lesions, more complicated lesions, and patients with acute coronary syndromes.[26,29,30,33,37] Therefore, the study populations of those studies were associated with a higher risk profile and consequently with an increased rate of adverse clinical outcomes. Notably, there have been few studies which have shown comparable results to our study regarding the mortality rate (4.3% and 4%).[27,32] Possibly, these studies included patients with milder renal impairment and therefore a better survival rate was found. In addition, Lemos et al have shown that renal impairment seems to be an independent predictor of mortality at one-year follow up after percutaneous coronary intervention (unadjusted hazard ratio 2.15, p=0.03), regardless of associated risk factors in this subset of patients.[30] In the present study our group of patients with CKD was not associated with a higher rate of comorbidities, apart from the increased prevalence of hypertension and advanced age.

Despite the higher mortality in patients with CKD, the impact of restenosis after DES implantation does not seem to be affected by the coexistence of CKD. Specifically, the rate of revascularisation in the present study was 2.08%, lower than in previous studies that reported a rate of target vessel revascularisation ranging from 4.0-7.0%.[27,30-32,37] These findings may support the hypothesis that renal disease is not correlated with the rate of target revascularisation due to restenosis. Hence, results from the use of DES in this particular subset of patients are similar to those in patients without CKD, as has already been demonstrated in previous large randomised studies.[8,10,38,39]

In the DES era, renal failure seems to be a significant risk factor for stent thrombosis.[40-42] The precise mechanism of stent thrombosis in renal impairment has not yet been well clarified. It is likely that the inflammatory process of renal impairment may cause a deterioration in vascular endothelium, platelet dysfunction and coagulopathy.[43,44] Thus, these factors may contribute to the increase in stent thrombosis in patients with renal disease.[43,44] Additionally, the resistance to or interruption of dual antiplatelet therapy may be a predictor of thrombosis.[45,46] Therefore, in patients who undergo percutaneous coronary intervention with DES implantation, dual antiplatelet therapy is mandatory for a long period.[47-49] However, in our study a trend towards an increased rate of total thrombosis in the CKD group was found (6.25%), as compared to the non-CKD group (2.63%). Interestingly, only one patient with angiographic stent thrombosis from the CKD group had discontinued the dual antiplatelet therapy. Consequently, according to the results of this study, the impact of the discontinuation of dual antiplatelet therapy does not seem to affect the thrombosis rate in CKD patients. On the other hand, and of particular interest, is the fact that the observed results may be explained by a low response to the dual antiplatelet therapy due to resistance to these substances. Genetic and acquired factors are implicated as a mechanism in the resistance to dual antiplatelet therapy.[50] This may necessitate an evaluation of platelet function prior to the administration of medication.

This was a single-centre study with a relatively small sample of patients. Nevertheless, the mid-term follow up and the prospective enrolment of patients allow us to reach safe conclusions regarding the treatment approach in patients suffering from CKD.

Conclusion

Percutaneous coronary intervention with new-generation DES in the pLAD of patients suffering from chronic stable angina with CKD is associated with increased mortality. However, the rates of target lesion revascularisation and angiographically documented thrombosis are comparable to those in patients with normal renal function. Thus, even in a low-risk population the severity of CKD should be considered prior to the procedure of DES implantation.

References

1. Klein LW, Weintraub WS, Agarwal JB, et al. Prognostic significance of severe narrowing of the proximal portion of the left anterior descending coronary artery. Am J Cardiol. 1986; 58: 42-46.
2. Kimura BJ, Russo RJ, Bhargava V, McDaniel MB, Peterson KL, DeMaria AN. Atheroma morphology and distribution in proximal left anterior descending coronary artery: in vivo observations. J Am Coll Cardiol. 1996; 27: 825-831.
3. Dangas G, Ellis SG, Shlofmitz R, et al. Outcomes of paclitaxel-eluting stent implantation in patients with stenosis of the left anterior descending coronary artery. J Am Coll Cardiol. 2005; 45: 1186-1192.
4. Khattab AA, Hamm CW, Senges J, et al. Incidence and predictors of target vessel revascularization after sirolimus-eluting stent treatment for proximal left anterior descending artery stenoses among 2274 patients from the prospective multicenter German Cypher Stent Registry. Clin Res Cardiol. 2007; 96: 279-284.
5. Lee CW, Tan C-H, Suh J, et al. Sirolimus-eluting stent implantation for treatment of proximal left anterior descending coronary artery lesions: long-term outcome and predictors of adverse cardiac events. Catheter Cardiovasc Interv. 2007; 70: 368-373.
6. Valencia J, Berenguer A, Mainar V, et al. Two-year follow-

up of sirolimus-eluting stents for the treatment of proximal left anterior descending coronary artery stenosis. J Interv Cardiol. 2006; 19: 126-134.
7. Bonello L, De Labriolle A, Lemesle G, et al. Comparison of outcomes of drug-eluting stents versus bare-metal stents in nonostial proximal left anterior descending coronary arteries. Am J Cardiol. 2009; 103: 496-500.
8. Beijk MA, Neumann F-J, Wiemer M, et al. Two-year results of a durable polymer everolimus-eluting stent in de novo coronary artery stenosis (The SPIRIT FIRST Trial). EuroIntervention. 2007; 3: 206-212.
9. Fajadet J, Wijns W, Laarman G-J, et al. Randomized, double-blind, multicenter study of the Endeavor zotarolimus-eluting phosphorylcholine-encapsulated stent for treatment of native coronary artery lesions: clinical and angiographic results of the ENDEAVOR II trial. Circulation. 2006; 114: 798-806.
10. Fajadet J, Wijns W, Laarman G-J, et al. Randomized, double-blind, multicenter study of the Endeavor zotarolimus-eluting phosphorylcholine-encapsulated stent for treatment of native coronary artery lesions. Clinical and angiographic results of the ENDEAVOR II Trial. Minerva Cardioangiol. 2007; 55: 1-18.
11. Ruygrok PN, Desaga M, Van Den Branden F, et al. One year clinical follow-up of the XIENCE V Everolimus-eluting stent system in the treatment of patients with de novo native coronary artery lesions: the SPIRIT II study. EuroIntervention. 2007; 3: 315-320.
12. Sakurai R, Hongo Y, Yamasaki M, et al. Detailed intravascular ultrasound analysis of Zotarolimus-eluting phosphorylcholine-coated cobalt-chromium alloy stent in de novo coronary lesions (results from the ENDEAVOR II trial). Am J Cardiol. 2007; 100: 818-823.
13. Serruys PW, Ong AT, Piek JJ, et al. A randomized comparison of a durable polymer Everolimus-eluting stent with a bare metal coronary stent: The SPIRIT first trial. EuroIntervention. 2005; 1: 58-65.
14. Fried LF, Shlipak MG, Crump C, et al. Renal insufficiency as a predictor of cardiovascular outcomes and mortality in elderly individuals. J Am Coll Cardiol. 2003; 41: 1364-1372.
15. Mann JF, Gerstein HC, Pogue J, Bosch J, Yusuf S. Renal insufficiency as a predictor of cardiovascular outcomes and the impact of ramipril: the HOPE randomized trial. Ann Intern Med. 2001; 134: 629-636.
16. Levin A, Djurdjev O, Barrett B, et al. Cardiovascular disease in patients with chronic kidney disease: getting to the heart of the matter. Am J Kidney Dis. 2001; 38: 1398-1407.
17. Best PJM, Lennon R, Ting HH, et al. The impact of renal insufficiency on clinical outcomes in patients undergoing percutaneous coronary interventions. J Am Coll Cardiol. 2002; 39: 1113-1119.
18. Hemmelgarn BR, Ghali WA, Quan H, et al. Poor long-term survival after coronary angiography in patients with renal insufficiency. Am J Kidney Dis. 2001; 37: 64-72.
19. Herzog CA, Ma JZ, Collins AJ. Long-term outcome of dialysis patients in the United States with coronary revascularization procedures. Kidney Int. 1999; 56: 324-332.
20. Kahn JK, Rutherford BD, McConahay DR, Johnson WL, Giorgi LV, Hartzler GO. Short- and long-term outcome of percutaneous transluminal coronary angioplasty in chronic dialysis patients. Am Heart J. 1990; 119: 484-489.
21. Papafaklis MI, Naka KK, Papamichael ND, et al. The impact of renal function on the long-term clinical course of patients who underwent percutaneous coronary intervention. Catheter Cardiovasc Interv. 2007; 69: 189-197.
22. Szczech LA, Reddan DN, Owen WF, et al. Differential survival after coronary revascularization procedures among patients with renal insufficiency. Kidney Int. 2001; 60: 292-299.
23. Xie D, Hou YQ, Hou FF, et al. Coronary stenting does not improve the long-term cardiovascular outcome of patients with mild to moderate renal insufficiency. Chin Med J (Engl). 2009; 122: 158-164.
24. Gruberg L, Dangas G, Mehran R, et al. Clinical outcome following percutaneous coronary interventions in patients with chronic renal failure. Catheter Cardiovasc Interv. 2002; 55: 66-72.
25. Rubenstein MH, Harrell LC, Sheynberg BV, Schunkert H, Bazari H, Palacios IF. Are patients with renal failure good candidates for percutaneous coronary revascularization in the new device era? Circulation. 2000; 102: 2966-2972.
26. Zhang Q, Zhang RY, Shen J, et al. Impact of admission creatinine level on clinical outcomes of patients with acute ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention with drug-eluting stent implantation. Chin Med J (Engl.) 2008; 121: 2379-2383.
27. Jeong Y-H, Hong M-K, Lee CW, et al. Impact of significant chronic kidney disease on long-term clinical outcomes after drug-eluting stent versus bare metal stent implantation. Int J Cardiol. 2008; 125: 36-40.
28. Jeong Y-H, Hong M-K, Park D-W, Lee C-W, Park S-W, Park S-J. Drug-eluting stent implantations in patients with chronic kidney disease are useful to reduce revascularization. Int J Cardiol 2009; 133: 247-248.
29. Hassani S-E, Chu WW, Wolfram RM, et al. Clinical outcomes after percutaneous coronary intervention with drug-eluting stents in dialysis patients. J Invasive Cardiol. 2006; 18: 273-277.
30. Lemos PA, Arampatzis CA, Hoye A, et al. Impact of baseline renal function on mortality after percutaneous coronary intervention with sirolimus-eluting stents or bare metal stents. Am J Cardiol. 2005; 95: 167-172.
31. Das P, Moliterno DJ, Charnigo R, et al. Impact of drug-eluting stents on outcomes of patients with end-stage renal disease undergoing percutaneous coronary revascularization. J Invasive Cardiol. 2006; 18: 405-408.
32. Halkin A, Mehran R, Casey CW, et al. Impact of moderate renal insufficiency on restenosis and adverse clinical events after paclitaxel-eluting and bare metal stent implantation: results from the TAXUS-IV Trial. Am Heart J. 2005; 150: 1163-1170.
33. Briguori C, Airoldi F, Chieffo A, Carlino M, Montorfano M, Colombo A. Renal function and drug-eluting stent. Int J Cardiol 2010; 142: 92-94.
34. Mehran R, Dangas G, Abizaid AS, et al. Angiographic patterns of in-stent restenosis: classification and implications for long-term outcome. Circulation. 1999; 100: 1872-1878.
35. Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation. 2007; 115: 2344-2351.
36. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002; 39: S1-266.
37. Kuchulakanti PK, Torguson R, Chu WW, et al. Impact of chronic renal insufficiency on clinical outcomes in patients undergoing percutaneous coronary intervention with sirolimus-eluting stents versus bare metal stents. Am J Cardiol. 2006; 97: 792-797.

38. Stone GW, Ellis SG, Cox DA, et al. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. N Engl J Med. 2004; 350: 221-231.
39. Schofer J, Schlüter M, Gershlick AH, et al. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-SIRIUS). Lancet. 2003; 362: 1093-1099.
40. Kuchulakanti PK, Chu WW, Torguson R, et al. Correlates and long-term outcomes of angiographically proven stent thrombosis with sirolimus- and paclitaxel-eluting stents. Circulation. 2006; 113: 1108-1113.
41. Machecourt J, Danchin N, Lablanche JM, et al. Risk factors for stent thrombosis after implantation of sirolimus-eluting stents in diabetic and nondiabetic patients: the EVASTENT Matched-Cohort Registry. J Am Coll Cardiol. 2007; 50: 501-508.
42. Iakovou I, Schmidt T, Bonizzoni E, et al. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. JAMA. 2005; 293: 2126-2130.
43. McCullough PA. Why is chronic kidney disease the "spoiler" for cardiovascular outcomes? J Am Coll Cardiol. 2003; 41: 725-728.
44. Luke RG. Chronic renal failure–a vasculopathic state. N Engl J Med. 1998; 339: 841-843.
45. McFadden EP, Stabile E, Regar E, et al. Late thrombosis in drug-eluting coronary stents after discontinuation of antiplatelet therapy. Lancet. 2004; 364: 1519-1521.
46. Buonamici P, Marcucci R, Migliorini A, et al. Impact of platelet reactivity after clopidogrel administration on drug-eluting stent thrombosis. J Am Coll Cardiol. 2007; 49: 2312-2317.
47. Silber S, Richartz BM, Brilmayer M. [The European Society of Cardiology (ESC) guidelines for percutaneous coronary interventions (PCI). Three case reports]. Herz. 2006; 31: 836-46, 848.
48. Kremastinos DT, Farmakis DT, Anastasiou-Nana M. Drug-eluting stents: where are we today? Hellenic J Cardiol. 2010; 51: 287-289.
49. Korovesis S, Katritsis DG. Stent thrombosis four and a half years after implantation of a sirolimus-eluting stent. Hellenic J Cardiol. 2009; 50: 423-425.
50. Geisler T, Gawaz M. [Resistance to antiplatelet substances--a real clinical problem]. Herz. 2008; 33: 260-268.