Journal of Zhejiang University-SCIENCE B (Biomedicine & Biotechnology) ISSN 1673-1581 (Print); ISSN 1862-1783 (Online) www.zju.edu.cn/jzus; www.springerlink.com E-mail: jzus@zju.edu.cn



### Complex coronary lesions and rotational atherectomy: one hospital's experience<sup>\*</sup>

Jun JIANG<sup>§1,2</sup>, Yong SUN<sup>§1,2</sup>, Mei-xiang XIANG<sup>1,2</sup>, Liang DONG<sup>1,2</sup>, Xian-bao LIU<sup>1,2</sup>,

Xin-yang  $\mathrm{HU}^{1,2},$  Yan FENG^{1,2}, Jian-an WANG^{\dagger\ddagger1,2}

(<sup>1</sup>Department of Cardiology, the Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310009, China) (<sup>2</sup>Cardiovascular Key Lab of Zhejiang Province, the Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310009, China)

<sup>†</sup>E-mail: Wang\_jian\_an@tom.com

Received June 26, 2012; Revision accepted July 7, 2012; Crosschecked July 6, 2012

**Abstract:** Objective: To evaluate the safety and effectiveness of rotational atherectomy followed by drug eluting stent (DES) implantation in patients with complex coronary lesions. Methods: From August 2006 to August 2012, 253 consecutive patients with 289 lesions and who underwent rotational atherectomy in our center were enrolled in this study. Results: The overall procedure success rate was 98% with the cost of two (0.8%) coronary perforations, three (1.2%) dissections, five (2.0%) slow flows or no flows, three (1.2%) peri-procedure myocardial infarctions, and two (0.8%) in hospital deaths. During follow-up (mean three years), one (0.4%) patient died, two (0.8%) patients had acute myocardial infarction, 14 (5.5%) had restenosis, and target lesion revascularization occurred in eight patients (3.2%). Conclusions: Rotational atherectomy followed by DES implantation is a safe and effective technique for patients with complex coronary lesions, especially calcified and non-dilatable lesions.

Key words: Complex coronary lesions, Calcified coronary lesions, Rotational atherectomy, Drug eluting stentsdoi:10.1631/jzus.B1201008Document code: ACLC number: R541.4

#### 1 Introduction

During the past decade, interventional cardiologists have encountered more and more challenging coronary cases, including calcified and chronic total occluded lesions, in patients with advanced age and multiple co-morbidities (chronic renal failure, etc.) and without good indications for coronary artery bypass graft (CABG) surgery. As shown in the Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital (RESEARCH) study, there have been more AHA/ACC type C lesions in the era of drug eluting stent (DES) compared with pre-DES times, 43% vs. 32% (P < 0.01) (Lemos *et al.*, 2004). Calcified lesions remain a unique challenge for all interventional cardiologists as they carry the risk of dissection during balloon dilation, may block stent delivery and lead to acute procedure failure (Camnitz and Keeley, 2010). DES has been proved to reduce the restenosis rate compared with bare metal stent (BMS) after percutaneous coronary intervention (PCI) (Pocock *et al.*, 2008). However, their efficacy and safety in calcified coronary lesions are less well established. Calcified coronary lesions may lead to stent under-expansion and malapposition, and increase rates of restenosis and stent thrombosis later on (Fujii *et al.*, 2004; Kawaguchi *et al.*, 2008).

Rotational atherectomy was first developed as a coronary interventional modality, such as directional coronary atherectomy and excimer laser coronary angioplasty (ELCA), to ablate plaque and open a

<sup>&</sup>lt;sup>‡</sup> Corresponding author

<sup>&</sup>lt;sup>§</sup> The two authors contributed equally to this work

<sup>\*</sup> Project (Nos. 2009C33123 and 2007C13058) supported by the Science and Technology Project of Zhejiang Province, China

<sup>©</sup> Zhejiang University and Springer-Verlag Berlin Heidelberg 2012

diseased artery. It differentially ablates hard calcified tissue or fibrotic plaque with high speed rotating burs and causes less injury to the elastic tissue. Unfortunately, rotational atherectomy has failed to prove superior to percutaneous transluminal coronary angioplasty (PTCA) or ECLA in terms of reducing the restenosis rate after intervention, but there was less crossover to PTCA or ECLA during the procedure (MacIsaac et al., 1995; Mauri et al., 2003). Nevertheless, rotational atherectomy is currently recommended for preparation of heavily calcified or severely fibrotic lesions that cannot be crossed by a balloon or adequately dilatated before planned stenting. In combination with DES, it might be an effective method to treat complex coronary lesions. Here we report the results of rotational atherectomy in these kinds of lesions in our center.

### 2 Materials and methods

Two hundred and fifty-three consecutive patients with complex coronary lesions and who underwent rotational atherectomy in our center from August 2006 to August 2012, were enrolled into this retrospective analysis. After written informed consents were obtained, we performed the procedure and inputted all the demographic, clinical, angiographic, and interventional data into our database. A loading dose of antiplatelet agents, including 300 mg aspirin and 300 mg clopidogrel, was given to all patients at least 12 h before the procedure, and an additional dose of 300 mg clopidogrel was given at the discretion of the operator, after the diagnostic angiogram.

Rotational atherectomy was performed with the Rotablator<sup>®</sup> Rotational Atherectomy System (Boston Scientific Corporation, Natick, MA, USA) through a radial or femoral approach. The 0.009 inch (1 inch= 2.54 cm) RotaWire<sup>®</sup> guide wire was introduced either directly across the lesion or exchanged with a workhorse guide wire such as Runthrough<sup>®</sup> NS (Terumo Medical Corporation, Somerset, NJ, USA) via a microcatheter. In most cases a step-up technique with two or three burrs was chosen in order to reduce the incidence of the no-reflow phenomenon. The size of first burr was usually 1.25 or 1.50 mm depending on the minimal residual lumen diameter of the lesions. The second burr was usually 1.50 or 1.75 mm since

the majority of our patients were treated through a transradial approach. Once the burr was advanced into the guiding catheter, a heparinised normal saline solution with nitroglycerine was infused locally to prevent overheating and vascular spasm, and to avoid the no-reflow phenomenon. A dyna-glide technique was used to advance the burr through a guiding catheter to reduce friction, and the atherectomy was performed using the pecking motion maneuver until all the way through the lesion, with an initial ablation speed of 140000-180000 r/min. The duration of rotational atherectomy application was 15-20 s, with immediate cessation if the speed dropped by >5000 r/min. Following successful modification of the plaque, a DES was implanted according to the vessel's size with or without adjunctive balloon pre-dilatation, at the operator's discretion. Six types of DES were used: the Taxus® stent (Boston Scientific, Natick MA, USA), Cypher® stent (Cordis, Miami Lakes FA, USA), Endeavor® stent (Medronic, Minneapolis MN, USA), Xience V<sup>®</sup> stent (Abbott, Park IL, USA), Excel® stent (JW Medical System, Weihai, China), and Partner<sup>®</sup> stent (Lepu Medical, Beijing, China). After stent implantation, postdilatation was performed with a non-compliant balloon at high pressure to ensure optimal stent apposition. Residual stenosis of <20% was considered an angiographic success.

Double antiplatelet therapy with clopidogrel (75 mg/d) and aspirin (100 mg/d) was administered for at least 12 months after intervention, as well as a  $\beta$  blocker and statin. Cardiac troponin I, creatinine kinase (CK), and creatine kinase-myocardial band isoenzyme (CK-MB) were recorded at 6 and 12 h post-procedure. Follow-up data included death from any cause, acute myocardial infarction, target lesion restenosis, new coronary lesions, and target lesion revascularization.

Statistical analysis was carried out using SPSS 15.0. Continuous variables are expressed as mean± standard deviation (SD), and categorical variables as number (percentage).

#### **3 Results**

#### 3.1 Baseline characteristics

The 253 patients enrolled into this study had a

mean age of 73 years. Sixty-nine percent were male, 66% had hypertension, 43% had hyperlipidemia, 25% had diabetes, and 16% of patients had an ejection fraction of <50% (Table 1). Eleven percent of patients were admitted due to acute myocardial infarction.

Table 1Baseline characteristics of 253 patients in ourstudy

Parameter	Value*
Age (year)	73±12
Men (%)	69
Hypertension (%)	66
Hyperlipidemia (%)	43
Diabetes mellitus (%)	25
Smoking (%)	30
Angina (%)	89
Acute myocardial infarction (%)	11
Ejection fraction <50% (%)	16
*Value are expressed as mean+SD or percents	nge

# 3.2 Angiographic findings and PCI procedure description

In this aged patient group, angiograms showed complex coronary lesions, with 53% type B2 and 30% type C lesions. The major indication for rotational atherectomy is calcified (72%) and balloon undilatable (19%) lesions, although a few cases with in-stent restenosis and chronic total occlusion underwent rotational atherectomy. The most frequently used burr size was 1.50 mm, and the mean burr/artery ratio was 0.55±0.08. After rotational atherectomy, 15% of the lesions proceeded directly to stenting without balloon pre-dilatation. DES implantation was successful in 100% of lesions with a 98% procedure success rate (Table 2). Some patients also underwent intravascular ultrasound (IVUS) examination to further evaluate the lesion calcification, guide the selection of stent diameter and length, and check whether the stents were fully expanded and well apposed to the vascular wall (Figs. 1 and 2).

## **3.3** In-hospital complications and major cardiac adverse events during follow-up

Procedural complications included two (0.8%) coronary perforations, both occurring after stent implantation with no direct association with rotational atherectomy; one was sealed with a membrane covered stent and the other received surgical repair; dissection resolved after DES implantation occurred in

three (1.2%) patients; there was no significant side (>1.50 mm) branch occlusion; and slow-flow or no flow occurred in five (2%) patients, and was temporary and corrected by intracoronary infusion of nitroglycerine or verapamil. Prophylactic pacemakers were implanted for right or left circumflex coronary artery lesions in our early phase but are no longer routinely implanted, because complete atrioventricular block or significant sinus bradycardia caused by rotational atherectomy is not so frequent and can easily be reversed with intravenous atropine.

Table 2Angiographic findings and PCI proceduredescription of 289 lesions

Parameter	Value*
	varae
Type of lesion	
А	23 (8%)
B1	25 (9%)
B2	154 (53%)
С	87 (30%)
Indication for rotational atherectomy	
Calcified lesions	208 (72%)
Undilatable lesions	55 (19%)
Bifurcation lesions	12 (4%)
In-stent restenosis	3 (1%)
Ostial lesions	3 (1%)
Chronic total occlusion	8 (3%)
Procedure success <sup>#</sup>	248 (98%)
Burr/artery ratio	$0.55 \pm 0.08$
Adjunctive balloon predilatation	246 (85%)
Stenting after rotational atherectomy	289
	(100%)

\* Data are expressed as n (%) or mean±SD; # total n=253

Regarding in-hospital major complications, no deaths occurred during the procedure. Two deaths occurred during hospitalization: one patient with coronary perforation caused by an over-sized stent and who received surgical repair died after 7 d due to persistent hypotension. Another patient (56 years old, acute diffuse anterior myocardial infarction with an ejection fraction of 32%, diseased distal left main (LM) and long left anterior descending artery (LAD) lesion, received PCI one month after onset of heart attack) developed no reflow, ventricular fibrillation and died of cardiogenic shock 8 h after stent implantation. Acute non Q wave myocardial infarction occurred in three (1.2%) patients with no significant clinical sequela. There was no emergent coronary artery bypass graft (CABG) after PCI.



**Fig. 1** Coronary angiogram (a–c) and IVUS (d–f) of an 82-year old man with calcified distal LM lesion The results showed severe stenosis in the distal LM with significant calcification in an 82-year old man with unstable angina, hypertension, diabetes, and right coronary intervention eight years ago (a, d). Rotational atherectomy with a 1.75 mm burr created a fissure in the endothelial calcification (b, e). The final angiogram showed well expanded and apposed DES, confirmed by IVUS examination (c, f)



Fig. 2 Rotational atherectomy and crush stenting in a 66-year old patient with LM bifurcation lesion after coronary artery bypass graft (CABG)

A 66-year old man was admitted due to recurrent chest pain following exertion for six years, and re-occurrence attacks for two months. Six years ago he suffered acute inferior myocardial infarction and received CABG with three vein grafts. Two months ago symptoms recurred and coronary CT angiogram (CTA) showed diffuse calcification in the LM (a) and its bifurcation with totally occluded vein grafts (b). Angiograms showed tight stenosis in the distal LM involving the proximal left anterior descending artery (LAD) and left circumflex coronary artery (LCX) (c). Double kissing crush stenting was performed (d) and the angina was resolved. Six months after the procedure, a routine follow-up angiogram found moderate in-stent restenosis only in the mid LAD (e, f), and focal stent malapposition caused by positive remodeling in the proximal LAD (white arrows in e)

The remaining 251 patients were followed up for a median time of three years after discharge. Two patients (0.8%) had acute myocardial infarction. One patient (78 years old, diffuse anterior myocardial infarction, ventricular aneurysm, three diseased vessels) died six months post-procedure. At the nine months follow-up, 185 (73.7%) of the surviving patients were given an angiogram, and the restenosis rate was 5.5%. The total target lesion revascularization (TLR) was 3.2% (Table 3).

Table 3 In-hospital complications and major adversecardiac events (MACE) during follow-up

Parameter	Number of patients*
Procedural complications	
Perforation	2 (0.8%)
Dissection	3 (1.2%)
Side branch occlusion	0
Slow-flow or no flow	5 (2.0%)
In-hospital major complications	
Acute myocardial infarction	3 (1.2%)
Death	2 (0.8%)
CABG	0
MACE during follow-up	
Acute myocardial infarction	2 (0.8%)
Restenosis	14 (5.5%)
TLR	8 (3.2%)
Death	1 (0.4%)

Data are expressed as n (%); CABG: coronary artery bypass graft; TLR: target lesion revascularization

### 4 Discussion

As China develops an aging society, interventional cardiologists here have to take care of more senile patients with multiple co-morbidities and complex coronary lesions, especially calcified coronary lesions. In our study group, patients had a mean age of 73 years, 66% had hypertension, 25% diabetes, and 83% type B2 and C coronary lesions, which is consistent with the results of the RESEARCH study (Lemos et al., 2004). Renal dysfunction is more common in an aged population. Calcified coronary lesions are more common in senile, diabetic, and chronic renal failure patients, and are associated with higher mortality (Stavroulopoulos et al., 2011; Shimoyama et al., 2012). Calcified coronary lesions represent an advanced stage in the

atherosclerotic process, whereby a soft plaque gradually develops into a fibrocalcific plaque. Although calcified atherosclerotic plaques were thought to be stable in the past, a recent study found that the presence of spotty calcification was associated with more extensive and diffuse coronary atherosclerosis and accelerated disease progression (Kataoka *et al.*, 2012). Thus, patients with calcified coronary lesions deserve more intensive and comprehensive treatment to improve their prognosis.

However, treatment of calcified lesions is challenging due to higher rates of procedural failure and complication, stent under-expansion and malapposition, elevated risk of restenosis and stent thrombosis (Virmani et al., 1994; Vavuranakis et al., 2001; Kawaguchi et al., 2008). In the PTCA era, calcified lesion was a significant predictor of major complications (Bredlau et al., 1985), as it carried the risk of dissection during balloon dilatation. DES has been proved to reduce the restenosis rate after PCI (Pocock et al., 2008). However, with its innate delayed endothelium coverage of stent struts, the efficacy and safety of DES in calcified coronary lesions cause more concern than those of BMS. Invented in the early 1980s by David Auth, rotational atherectomy differentially ablates hard calcified tissue or fibrotic plaque and causes less injury to the elastic tissue (MacIsaac et al., 1995). Over the past decade, rotational atherectomy has fallen out of favor primarily due to its relatively complicated manipulation process, lack of superiority in reducing restenosis rate compared with PTCA, and most importantly because improved deliverability has allowed a new generation of DES to be successfully implanted in complex coronary lesions, including calcified lesions. More recently, however, use of this modality has been revisited with a focus on its role in modifying calcified and non-dilatable coronary lesions to create a smooth pathway for stent delivery, reducing the rigid plaque burden, resulting in better stent deployment and apposition (Tran et al., 2008), and hopefully reducing the major adverse cardiac events (MACE) rate after the procedure.

In our study, rotational atherectomy followed by DES implantation produced 98% of procedure success with a low rate of complications, including 0.8% coronary perforation, 2.0% slow-flow or no flow, 0.8% in-hospital death, and 1.2%

peri-procedure myocardial infarction. During the mean three years of follow-up, 0.8% of patients had acute myocardial infarction, 0.4% died, 5.5% had 3.2% restenosis. and had target lesion revascularization. These results coincide well with those from recent published studies (Bangalore et al., 2011; Benezet et al., 2011; Dardas et al., 2011). Based on our experience, complications and MACE rates could be reduced by: increasing burr size step by step, using a reasonable burr/artery ratio (0.5–0.7), maintaining systolic blood pressure at ≥100 mmHg during the procedure, allowing enough time for observing coronary flow between two rotations, applying routine post-dilatation with non-compliant balloons, and using IVUS guidance for high risk patient subsets such as those with left main disease.

The main limitation of the present study was its retrospective design, lack of a control group and the angiographic absence of а full follow-up. Nevertheless, this study clearly indicates that rotational atherectomy plus DES implantation is a safe and effective strategy for patients with complex coronary lesions. Further randomized controlled trials are needed to explore fully the role of rotational atherectomy and DES implantation in patients with calcified coronary lesions, and the significance of new imaging modalities such as IVUS and optical coherence tomography in assessing and guiding the intervention of these kinds of lesions.

### References

- Bangalore, S., Vlachos, H.A., Selzer, F., Wilensky, R.L., Kip, K.E., Williams, D.O., Faxon, D.P., 2011. Percutaneous coronary intervention of moderate to severe calcified coronary lesions: insights from the National Heart, Lung, and Blood Institute Dynamic Registry. *Catheter. Cardiovasc. Interv.*, 77(1):22-28. [doi:10.1002/ccd.22613]
- Benezet, J., Diaz de la Llera, L.S., Cubero, J.M., Villa, M., Fernandez-Quero, M., Sanchez-Gonzalez, A., 2011. Drug-eluting stents following rotational atherectomy for heavily calcified coronary lesions: long-term clinical outcomes. J. Invasive Cardiol., 23(1):28-32.
- Bredlau, C.E., Roubin, G.S., Leimgruber, P.P., Douglas, J.S.Jr., King, S.B.3rd, Gruentzig, A.R., 1985. In-hospital morbidity and mortality in patients undergoing elective coronary angioplasty. *Circulation*, 72(5):1044-1052.
- Camnitz, W.M., Keeley, E.C., 2010. Heavily calcified coronary arteries: the bane of an interventionalist's existence. *J. Interv. Cardiol.*, 23(3):254-255. [doi:10.1111/j.1540-8183.2010.00553.x]
- Dardas, P., Mezilis, N., Ninios, V., Tsikaderis, D., Theofilo-

giannakos, E.K., Lampropoulos, S., 2011. The use of rotational atherectomy and drug-eluting stents in the treatment of heavily calcified coronary lesions. *Hellenic. J. Cardiol.*, **52**(5):399-406.

- Fujii, K., Mintz, G.S., Kobayashi, Y., Carlier, S.G., Takebayashi, H., Yasuda, T., Moussa, I., Dangas, G., Mehran, R., Lansky, A.J., *et al.*, 2004. Contribution of stent underexpansion to recurrence after sirolimus-eluting stent implantation for in-stent restenosis. *Circulation*, **109**(9): 1085-1088. [doi:10.1161/01.CIR.0000121327.67756.19]
- Kataoka, Y., Wolski, K., Uno, K., Puri, R., Tuzcu, E.M., Nissen, S.E., Nicholls, S.J., 2012. Spotty calcification as a marker of accelerated progression of coronary atherosclerosis: insights from serial intravascular ultrasound. J. Am. Coll. Cardiol., 59(18):1592-1597. [doi:10.1016/j. jacc.2012.03.012]
- Kawaguchi, R., Tsurugaya, H., Hoshizaki, H., Toyama, T., Oshima, S., Taniguchi, K., 2008. Impact of lesion calcification on clinical and angiographic outcome after sirolimus-eluting stent implantation in real-world patients. *Cardiovasc. Revasc. Med.*, 9(1):2-8. [doi:10.1016/j. carrev.2007.07.004]
- Lemos, P.A., Hoye, A., Goedhart, D., Arampatzis, C.A., Saia, F., van der Giessen, W.J., McFadden, E., Sianos, G., Smits, P.C., Hofma, S.H., *et al.*, 2004. Clinical, angiographic, and procedural predictors of angiographic restenosis after sirolimus-eluting stent implantation in complex patients: an evaluation from the Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital (RESEARCH) study. *Circulation*, **109**(11):1366-1370. [doi:10.1161/01.CIR.0000121358.26097.06]
- MacIsaac, A.I., Bass, T.A., Buchbinder, M., Cowley, M.J., Leon, M.B., Warth, D.C., Whitlow, P.L., 1995. High speed rotational atherectomy: outcome in calcified and noncalcified coronary artery lesions. *J. Am. Coll. Cardiol.*, 26(3):731-736. [doi:10.1016/0735-1097(95)00206-J]
- Mauri, L., Reisman, M., Buchbinder, M., Popma, J.J., Sharma, S.K., Cutlip, D.E., Ho, K.K., Prpic, R., Zimetbaum, P.J., Kuntz, R.E., 2003. Comparison of rotational atherectomy with conventional balloon angioplasty in the prevention of restenosis of small coronary arteries: results of the Dilatation vs. Ablation Revascularization Trial Targeting Restenosis (DART). Am. Heart J., 145(5):847-854. [doi:10.1016/S0002-8703(03)00080-2]
- Pocock, S.J., Lansky, A.J., Mehran, R., Popma, J.J., Fahy, M.P., Na, Y., Dangas, G., Moses, J.W., Pucelikova, T., Kandzari, D.E., *et al.*, 2008. Angiographic surrogate end points in drug-eluting stent trials: a systematic evaluation based on individual patient data from 11 randomized, controlled trials. *J. Am. Coll. Cardiol.*, **51**(1):23-32. [doi:10.1016/j.jacc.2007.07.084]
- Shimoyama, Y., Tsuruta, Y., Niwa, T., 2012. Coronary artery calcification score is associated with mortality in Japanese hemodialysis patients. *J. Ren. Nutr.*, **22**(1):139-142. [doi:10.1053/j.jrn.2011.10.024]
- Stavroulopoulos, A., Porter, C.J., Pointon, K., Monaghan, J.M., Roe, S.D., Cassidy, M.J., 2011. Evolution of coronary

artery calcification in patients with chronic kidney disease Stages 3 and 4, with and without diabetes. *Nephrol. Dial. Transplant.*, **26**(8):2582-2589. [doi:10.1093/ndt/gfq751]

- Tran, T., Brown, M., Lasala, J., 2008. An evidence-based approach to the use of rotational and directional coronary atherectomy in the era of drug-eluting stents: when does it make sense? *Catheter. Cardiovasc. Interv.*, **72**(5): 650-662. [doi:10.1002/ccd.21676]
- Vavuranakis, M., Toutouzas, K., Stefanadis, C., Chrisohou, C., Markou, D., Toutouzas, P., 2001. Stent deployment in

calcified lesions: can we overcome calcific restraint with high-pressure balloon inflations? *Catheter. Cardiovasc. Interv.*, **52**(2):164-172. [doi:10.1002/1522-726X(200102) 52:2<164::AID-CCD1041>3.0.CO;2-S]

Virmani, R., Farb, A., Burke, A.P., 1994. Coronary angioplasty from the perspective of atherosclerotic plaque: morphologic predictors of immediate success and restenosis. *Am. Heart J.*, **127**(1):163-179. [doi:10.1016/ 0002-8703(94)90522-3]

### Recommended papers related to this topic

### Effects of atorvastatin on progression of diabetic nephropathy and local RAGE and soluble RAGE expressions in rats

Authors: Lin Lu, Wen-hui Peng, Wei Wang, Ling-jie Wang, Qiu-jing Chen, Wei-feng Shen doi: 10.1631/jzus.B1101004 *J. Zhejiang Univ.-Sci B (Biomed & Biotechnol)*, 2011 Vol.12 No.8 P.652-659

**Abstract:** Objective: Advanced glycation end-products (AGEs) exert inflammatory and oxidative stress insults to produce diabetic nephropathy mainly through the receptor for AGEs (RAGE). This study aimed to assess the effect of atorvastatin on diabetic nephropathy via soluble RAGE (sRAGE) and RAGE expressions in the rat kidney. Methods: Thirty-two male Sprague-Dawley rats were divided into four groups based on the presence or absence of streptozotocin-induced diabetes with or without atorvastatin treatment (10 mg/kg for 24 weeks). Serum sRAGE and glycated albumin (GA) levels were measured with enzyme-linked immunosorbent assay (ELISA) and improved bromocresol purple methods. Renal AGEs, RAGE, endogenous secretory RAGE (es-RAGE), and sRAGE were determined with reverse transcription-polymerase chain reaction (RT-PCR) and Western blotting. Results: Mesangial expansion and microalbuminuria were aggravated in diabetic rats, and improved with atorvastatin treatment. Serum sRAGE levels were up-regulated, while renal RAGE expression was decreased in diabetic rats, associated with a reduction in accumulation of AGEs, though renal esRAGE mRNA expression was not significantly increased. Conclusions: Atorvastatin exerted a beneficial effect on diabetic nephropathy with reduced AGE accumulation, down-regulating RAGE expression and up-regulating sRAGE in the kidney.