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Interventional Cardiology

A Randomized Trial Comparing the Impact of a Nonionic (Iomeprol) Versus an Ionic (Ioxaglate) Low Osmolar Contrast Medium on Abrupt Vessel Closure and Ischemic Complications After Coronary Angioplasty

Rainer Schräder, MD, Ingo Esch, Roland Ensslen, MD, Wolf Andreas Fach, MD, Hartmut Merle, MD, Detlef Scherer, MD, Horst Sievert, MD, Hans Friedrich Spies, MD, Harald E. Zeplin, MD*

Frankfurt am Main, Germany

OBJECTIVES To assess the effect of nonionic versus ionic contrast media on abrupt vessel closure and major ischemic complications after coronary angioplasty.

BACKGROUND There is a continuous debate about the "thrombogenic potential" of nonionic contrast media. The results of both in vitro and in vivo investigations are incongruent.

METHODS We prospectively evaluated the outcomes of 2,000 patients undergoing percutaneous transluminal coronary angioplasty (PTCA). According to a randomized, double-blind protocol, they received either iomeprol (nonionic; n = 1,001) or ioxaglate (ionic; n = 999). Intracoronary thrombus before PTCA was found more often in the iomeprol group (4.2% vs 2.7%, p = 0.04). No other significant differences between both groups were observed with regard to pre-PTCA clinical and angiographic characteristics.

RESULTS The frequency of reocclusions necessitating repeat angioplasty occurring either in laboratory (2.9% with iomeprol and 3.0% with ioxaglate) or out of laboratory (3.1% vs 4.1%) was not significantly different. The rate of major ischemic complications was also comparable after both contrast media (emergency bypass surgery: 0.8% vs 0.7%, myocardial infarction: 1.8 vs 2.0%, cardiac death during hospital stay: 0.2% vs 0.2%). In the iomeprol group, more patients had dissections post-PTCA (30.2% vs 25.0%, p = 0.01) and more patients received intracoronary stents (31.6% vs 25.7%, p = 0.004). Allergic reactions requiring treatment occurred only in the ioxaglate group (0.0% vs 0.9%, p = 0.002).

CONCLUSIONS The nonionic contrast medium was not associated with a higher rate of abrupt vessel closure requiring repeat angioplasty, or major ischemic events. These data suggest that nonionic contrast media do not increase the risk of thrombotic complications in patients undergoing coronary interventions. (J Am Coll Cardiol 1999;33:395–402) © 1999 by the American College of Cardiology

Under in vitro conditions, contrast media have multiple effects on both the intrinsic and extrinsic pathway of blood coagulation, thrombocyte function and vascular endothelium. All contrast agents act as anticoagulants to a variable extent. Nonionic contrast media have a markedly lower inhibition of the intrinsic pathway (1–8). The discussion regarding the relationship between nonionic contrast media and thrombotic complications began when Robertson observed blood clot formation in angiographic syringes filled with a mixture of nonionic contrast medium and blood that were left stagnant for 30 min (9). Reports of thrombotic events occurring during diagnostic coronary angiography with nonionic contrast media have fueled the debate with additional concern (10). In an editorial published in 1990, Fareed et al. even postulated a "thrombogenic potential" of nonionic contrast media (11).

This has led to the concern that thrombus formation, abrupt vessel closure and major adverse cardiac events after coronary angioplasty may occur more often with nonionic than with ionic agents. Thus far, six randomized studies

From the Cardioangiologisches Centrum Bethanien, Frankfurt am Main; and *CardioCliniC, Frankfurt am Main, Germany.

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All authors have been involved in the conception and design of the study. Seven interventional cardiologists (Roland Ensslen, Wolf-Andreas Fach, Hartmut Merle, Detlef Scherer, Rainer Schräder, Horst Sievert, and Hans-Friedrich Spies) have performed the 2,000 PTCA procedures. Harald E. Zeplin, as a cardiovascular surgeon, provided surgical standby, and performed the emergent bypass operations. The chief technician of the catheterization laboratory (Ingo Esch) was responsible for randomization, data processing and statistical analysis. All authors have critically interpreted the data, and have revised and finally approved the manuscript for important intellectual content.

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Abbreviations and Acronyms

ASA	= acetyl salicylic acid
CK	= creatine kinase
Closure i.lab.	= abrupt vessel closure in laboratory
Closure o.lab.	= abrupt vessel closure out of laboratory
ECG	= electrocardiogram
g.w.	= guidewire
i.c.	= intracoronary
MACE	= major adverse cardiac events
MI	= myocardial infarction
NS	= not significant
Ref.	= reference
PTCA	= percutaneous transluminal coronary angioplasty

comparing the effects of nonionic versus ionic contrast media have been published (12–17). However, there were no significant differences observed in the incidence emergent bypass surgery, myocardial infarction and cardiac death between both types of contrast media. We have designed a trial to investigate prospectively whether the so called "thrombogenic potential" of nonionic contrast media may affect angiographic and clinical outcomes in patients undergoing both routine and high-risk coronary angioplasty.

METHODS

Patients and contrast media. All patients presenting for either elective or emergency coronary angioplasty at a single institution were considered eligible for randomization unless they had a known history of allergic reactions to iodinated contrast media. The protocol had been approved by the institutional review board on clinical research, and informed written consent was obtained from each patient before enrollment. Over a 14-month period (from January 1996 to February 1997), a total of 2,458 coronary interventions were performed in our catheterization laboratory. During that period, 2,000 patients were randomized to receive either iomeprol (Imeron 350, 350 mg iodine/ml, 0.62 osmol/kg; Bracco-Byk-Gulden GmbH, Konstanz, Germany; n = 1001), or ioxaglate (Hexabrix 320, 320 mg iodine/ml, 0.60 osmol/kg; Guerbet GmbH, Sulzbach/Taunus, Germany; n = 999). Of these 2,000 patients, 1,626 presented for elective interventions. Urgent PTCA (within 24 h) was performed in 346 patients with unstable angina. Emergent PTCA (within 1 h) was performed in 32 patients with acute myocardial infarction. The remaining 458 patients were not included because of known contrast allergy (n = 131) or because they refused randomization (n = 327). The baseline clinical data for each patient were recorded on standard forms.

Study protocol. During the entire study period, patients were randomized day by day (Monday through Sunday) before catheterization using a computer-generated randomization list kept by the chief technician (I.E.) in the laboratory. Coronary interventions were performed by seven interventional cardiologists (R.E., W.A.F., H.M., D.S., R.S., H.S., H.F.S.), who were blinded to the contrast agent by wrapping the bottle with an opaque plastic bag. The patients who were not on oral aspirin before PTCA received an intravenous injection of 500 mg soluble ASA before the intervention. Routinely, the patients received an intraarterial bolus injection of 20,000 units of heparin. Patients who had an intravenous 1,000-unit/h infusion of heparin before PTCA received a bolus of only 10,000 units. An additional bolus of 10,000 units of heparin was administered when considered necessary by the catheterization physician. The activated clotting time was not determined routinely. PTCA was performed using standard techniques through 6- and 8-French guiding catheters. The use of adjunctive techniques (intracoronary fibrinolysis, rotational and directional atherectomy, laser) was left to the discretion of the operator. Glycoprotein IIb/IIIa inhibitors were not utilized during any of these procedures. The criteria for the use of either primary (eg, restenosis, major dissection, recoil) or bail-out stent implantation were not predefined as part of the initial study design. The clinical decision for the use of stents was left to the discretion of the operator. Stent implantations were performed with high-pressure balloon inflations, and thereafter 250 mg ticlopidine twice daily was prescribed for 4 weeks, routinely. For abrupt vessel closure, urgent repeat coronary angioplasty was, in general, the initial strategy. Pre- and postprocedural electrocardiograms (ECGs) were recorded in all patients.

Procedural variables. The number of attempted lesions (n), fluoroscopy time (min), heparin dose (IU/kg) and the volume of contrast medium used (ml) were recorded together with eventual side effects requiring specific treatment.

Angiographic analysis. Coronary angiography was performed before and after balloon inflation, using at least two identical views for comparison. In grading the complexity of the lesions, the ACC/AHA (American College of Cardiology/American Heart Association) system of Ellis et al. (18) was used. The angioplasty procedure was defined as successful when the residual stenosis was less than 50% by visual assessment. Two independent operators reviewed the films for the pre- and postprocedural degree of stenosis, elastic recoil (immediate success after balloon inflation but residual stenosis >50% on the following angiograms), dissection, intracoronary thrombus and abrupt vessel closure. In case of disagreements between the two operators, the results were discussed and a third operator made the decision, when necessary.

Clinical endpoints. Primary endpoints were abrupt vessel closure occurring either during the percutaneous transluminal coronary angioplasty (in laboratory), defined as an intracoronary filling defect after balloon inflation causing total occlusion of the vessel and necessitating reintroduction of the balloon catheter, or after the procedure (out of

Table 1. Baseline Characteristics, Indication for PTCA and Lesion Morphology

	Iomeprol (n = 1,001)	Ioxaglate (n = 999)	p
Baseline Characteristics			
Age (years) (mean ± SD)	63.2 ± 10.0	63.3 ± 10.2	0.75
Male patients (%)	80.8	78.5	0.20
Weight (kg) (mean ± SD)	79.6 ± 12.5	78.9 ± 12.2	0.19
Prior myocardial infarction (%)	10.9	9.5	0.34
Prior bypass surgery (%)	9.1	8.1	0.47
Indication for PTCA			
Acute myocardial infarction (%)	1.6	1.6	1.00
Unstable angina (%)	17.9	16.7	0.52
Stable angina (%)	59.3	62.1	0.18
Silent ischemia (%)	14.5	14.2	0.85
Restenosis (%)	14.0	12.0	0.54
Lesion Morphology			
ACC/AHA Type A (%)	31.0	31.8	0.70
ACC/AHA Type B (%)	47.5	47.2	0.93
ACC/AHA Type C (%)	21.5	21.0	0.73
Thrombus before PTCA (%)	4.2	2.7	0.04
Dissection before PTCA (%)	1.3	1.4	0.85
Total occlusion (%)	12.4	12.4	1.00

laboratory), defined as an episode of ischemic chest pain and/or ST-segment changes, followed by the same angiographic finding. Secondary endpoints were major adverse cardiac events occurring during the patient's hospital stay for the PTCA procedure: emergency coronary bypass surgery, defined as the need for operative revascularization on the same day as the procedure for unstable or ongoing myocardial ischemia; myocardial infarction, defined either as an increase of the creatine kinase level above three times the upper limit of normal for our laboratory or the appearance of new Q-waves after the procedure; and cardiac death that occurred during the hospitalization.

Statistical analysis. Assuming an event rate of 5% in the control group, a difference of more than 3.2% in the other group would be detected to be statistically significant with a sample size of 1,000 patients in each arm ($p < 0.05$, power, 0.80). Data entry and data analysis were carried out using the software package SAS. Statistical comparison of differences between both groups were carried out using the Fisher exact test. A subgroup analysis was performed in patients with stable versus unstable coronary syndromes as well as in patients who received intracoronary stents versus patients who did not, although intracoronary stenting had not been predefined as an endpoint in the initial study design. For the primary and secondary clinical endpoints, the point estimates and 95% confidence limits among the patient subgroups were calculated.

RESULTS

Patients, indications for PTCA and lesion morphology. The baseline demographic data, the indication for PTCA and the morphology of target lesions in the nonionic and ionic contrast medium groups were similar. However, there were more patients with intracoronary thrombus pre-PTCA in the nonionic group (Table 1).

Procedural variables and angiographic outcomes. Atherectomy, both rotational and directional, and laser were used in less than 3% of patients in either contrast medium group. The fluoroscopy time and the contrast dose were comparable in the nonionic and the ionic group. The heparin dose was higher in patients randomized to receive the ionic contrast medium. In the nonionic group, more coronary lesions were attempted and more patients received thrombolytics. After balloon inflation, dissections and elastic recoil were observed significantly more often in patients randomized to the nonionic contrast medium. The incidence of intracoronary thrombi decreased in the nonionic group from 4.2% before PTCA to 2.8% after PTCA, but increased from 2.7% to 2.8% with the ionic contrast medium. Significantly more patients randomized to the nonionic contrast medium group received coronary stents. The success rate and the residual stenosis were similar in both groups (Table 2).

Adverse side effects. Allergic symptoms requiring therapy with either H_1- and H_2-antagonists and prednisolone or intravenous volume substitution and catecholamines were observed only in patients (n = 9) who were randomized to receive ioxaglate (bronchospasm = 1; vomiting = 1; rash = 3; hypotension = 4). The difference between both contrast media groups was significant ($p = 0.002$). Arrythmia requiring treatment (atropine, antiarrythmic drugs, defibrillation) occurred in two patients in the nonionic group (atrial fibrillation) compared with eight patients in the ionic group (bradycardia = 4; atrial fibrillation = 2; ventricular fibrillation = 2).

Table 2. Procedural Variables and Angiographic Outcomes

	Iomeprol (n = 1,001)	Ioxaglate (n = 999)	p
Procedural Variables			
Attempted coronary lesions	1,256	1,185	
Fluoroscopy time (min) (mean ± SD)	12.3 ± 11.4	12.2 ± 11.4	0.16
Heparin dose (IU/kg bw) (mean ± SD)	254 ± 47	258 ± 44	0.03
Contrast dose (ml/kg bw) (mean ± SD)	2.25 ± 1.0	2.28 ± 1.0	0.52
Intracoronary thrombolytics (%)	1.4	0.4	0.03
Stent implantation (%)	31.6	25.7	0.004
Angiographic Outcomes			
Successful PTCA (%)	92.6	92.4	0.87
Residual stenosis (% ± SD)	22.2 ± 24.8	21.3 ± 24.4	0.37
Elastic recoil (%)	4.6	2.8	0.04
Dissection (%)	30.2	25.0	0.01
Intracoronary thrombus (%)	2.8	2.8	1.00

Angiographic and clinical endpoints. There were no significant differences among both contrast medium groups. The primary endpoints were reached in 60 patients (6.0%) randomized to receive the nonionic contrast medium and in 71 patients (7.1%) in the ionic contrast medium group. Major adverse cardiac events were observed in 23 patients (2.3%) receiving the nonionic as well as the ionic contrast medium. There were two noncardiac deaths during the same hospital stay in the nonionic group. Both patients died after abdominal cancer surgery, 21 and 31 days after uncomplicated and successful coronary angioplasty, respectively (Table 3).

Patients with stable versus unstable symptoms. There were no significant differences between both contrast medium groups with regard to baseline demographic data, target vessels and target lesion morphology, except for the higher presence of thrombus before PTCA in the nonionic group (1.6% vs 1.0% in stable patients, and 10.5% vs 7.7% in unstable patients). Intracoronary stenting was performed more often in the nonionic group (28.6% vs 24.8% in stable patients, and 44.0% vs 29.8% in unstable patients). However, more dissections were observed after balloon angioplasty in patients randomized to receive the nonionic agent (28.6% vs 23.2% in stable patients, and 36.8% vs 33.1% in unstable patients). Between both contrast media, there were no significant differences with regard to abrupt closure in laboratory, abrupt closure out of laboratory or major adverse cardiac events neither in patients with stable nor in patients with unstable symptoms (Figs. 1–3).

Patients without and with intracoronary stents. No significant differences between both contrast medium groups with regard to baseline demographic data, target vessels, target lesion morphology and procedural variables were observed in the patients without stents. The incidence of post-PTCA thrombus, dissection and recoil was 1.8%, 14.2% and 1.6% in the nonionic, as compared with 2.0%, 10.6% and 1.2% in the ionic contrast medium group. In the patients who had received intracoronary stents, the incidence of pre-PTCA thrombus was 6.1% in the nonionic and 3.6% in the ionic contrast medium group. After balloon angioplasty (before stent implantation), the incidence of thrombus, dissection and recoil was 5.1%, 64.9% and 11.1% in the nonionic, as compared with 5.1%, 66.5% and 7.4% in the ionic contrast medium group. No significant differences between both contrast media groups were found with regard to abrupt closure in laboratory, abrupt closure out of laboratory or major adverse cardiac events neither in patients without nor in patients with intracoronary stents (Figs. 1–3).

Table 3. Clinical Endpoints

Clinical Endpoints	Iomeprol (n = 1,001)	Ioxaglate (n = 999)	p
Abrupt closure in laboratory (%)	29 (2.9)	30 (3.0)	0.90
Abrupt closure out of laboratory (%)	31 (3.1)	41 (4.1)	0.23
Emergency bypass surgery (%)	8 (0.8)	7 (0.7)	0.82
Myocardial infarction, CK increase (%)	11 (1.1)	11 (1.1)	1.00
Myocardial infarction, Q-wave (%)	7 (0.7)	9 (0.9)	0.63
Cardiac death (%)	2 (0.2)	2 (0.2)	1.00
Major adverse cardiac events	28	29	
Patients with MACE (%)	23 (2.3)	23 (2.3)	1.00

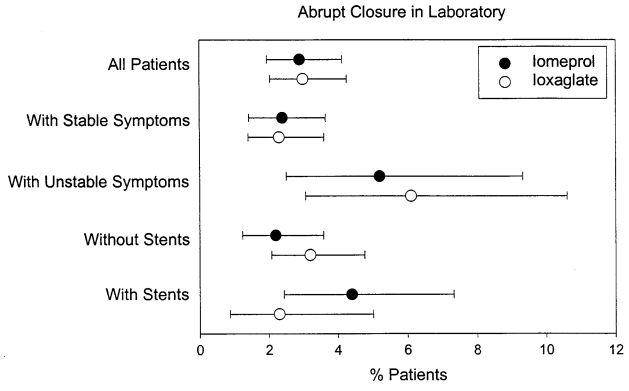

Figure 1. Point estimates of percent patients and 95% confidence limits for abrupt closure in laboratory among the patient subgroups.

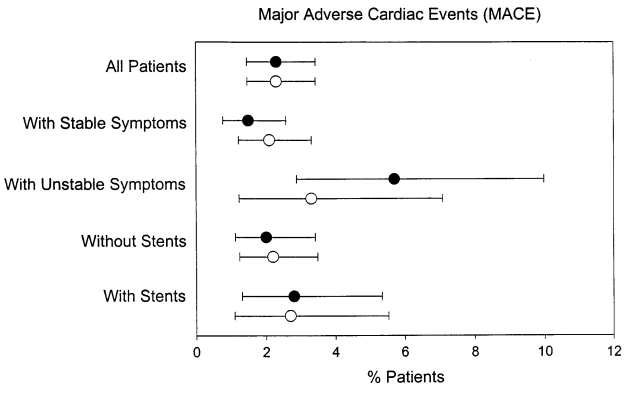

Figure 3. Point estimates of percent patients and 95% confidence limits for major adverse cardiac events among the patient subgroups.

DISCUSSION

Coronary angioplasty, abrupt vessel closure and major adverse cardiac events. Abrupt vessel closure, usually associated with flow-limiting intimal flaps or medial dissections after coronary angioplasty, has remained an important complication since PTCA was introduced by Grüntzig et al. in 1977 (19). Depending on the definition employed, the reported incidence has been variable, ranging from 2.0% to 8.3% and, notably, has not appreciably diminished over the past two decades (20–22). The most common angiographic feature is that of obstructive coronary dissection, with an incidence ranging from 35% to 80% (23). The presence of intraluminal thrombus has been detected in up to 44% of patients with coronary occlusion, often superimposed upon medial dissection (24).

There are many factors, both clinical (coronary anatomy, myocardium at risk, lesion morphology, stable/unstable angina/acute myocardial infarction) and technical (pretreatment with aspirin, heparin dose, use of glycoprotein IIb/IIIa inhibitors and stents) that may affect the incidence of abrupt closure and major ischemic events after coronary angioplasty. These considerations outline the difficulties in comparing the outcomes of trials that have been designed to investigate the effects of nonionic and ionic contrast media on abrupt vessel closure and ischemic complications after coronary angioplasty.

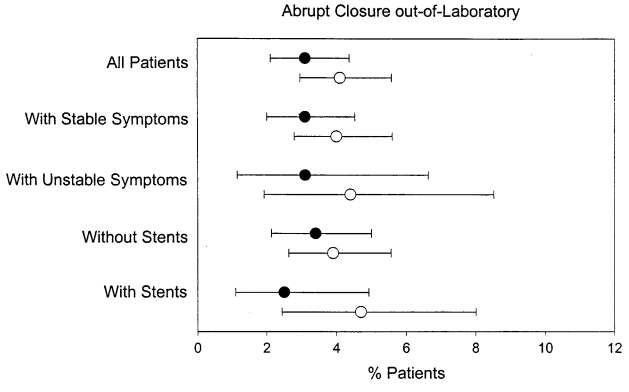

Figure 2. Point estimates of percent patients and 95% confidence limits for abrupt closure out-of-laboratory among the patient subgroups.

Previous reports on nonionic versus ionic contrast media and PTCA complications. Thus far, six randomized prospective clinical trials comparing nonionic and ionic contrast media in patients undergoing both elective and emergency coronary angioplasty have been published (Table 4). In four of these trials, the incidence of abrupt vessel closure, coronary thrombosis or platelet deposition on guide wire was lower with the ionic contrast medium (13–15,17). No significant differences with respect to major ischemic complications were observed between both types of contrast media in five of these six trials (12–15,17). Only in one study was a significant difference in post-PTCA ischemic events observed; despite a comparable angiographic outcome in both groups, the need for urgent recatheterization ($p = 0.02$) and re-PTCA ($p = 0.06$) was less frequent in patients allocated to receive the ionic agent (16).

Comparison with present data. More patients were enrolled in the present study than in the six previously published trials combined ($n = 1,963$). In these 2,000 patients undergoing predominantly elective coronary angioplasty, the incidence of abrupt vessel closure (events occurring in laboratory and out of laboratory combined) was 6.5%, and the incidence of major ischemic complications (myocardial infarction, emergent bypass surgery and cardiac death combined) was 2.8%. Except for severe allergic reactions requiring therapy that occurred only after the ionic compound, there were no significant differences between patients randomized to receive either the nonionic contrast medium (iomeprol) or the ionic agent (ioxaglate).

In consideration of the baseline clinical and angiographic data, the patients enrolled in the present study were closely comparable with the patient population of Piessens et al.

Table 4. Randomized Trials Comparing the Effects of Ionic Versus Nonionic Contrast Media in Patients Undergoing Coronary Angioplasty

Author Year Ref.	Contrast Medium	Patients Ionic Nonionic	Stable Unstable Acute MI	Heparin Dose (IU)	Endpoints	Patients (n) With Endpoints Ionic vs/Nonionic	p Values Ionic vs. Nonionic	Conclusion of the Authors
Lembo		PTCA = 1058	22.6%	10,000 bolus	arrythmia	14 vs 5	0.045	"... nonionic contrast medium reduces
1991	diatrizoate	n = 507	74.3%	5,000 after > 1 h	allergy	0 vs 1	NS	overall incidence of serious ventricular
#12	iopamidol	n = 551	3.1%		MACE	55 vs 55	NS	arrhythmias but not the frequency of myocardial infarction, the need for surgery, or death."
Esplugas		n = 100	32%	10,000 Bolus	thrombus i.c.	1 vs 11	< 0.005	... ", compared with ... ioxaglate, the
1991	ioxaglate	n = 50	68%	2,500 after > 2 h	thrombus g.w.	1 vs 6	NS	nonionic low osmolar contrast agent
#13	iohexol	n = 50	0%		MACE	1 vs 2	NS	iohexol increases the incidence of thrombus during coronary angioplasty."
Piessens		n = 500	60%	10,000 Bolus	Closure i.lab.	8 vs 18	0.044	"With multivariate analysis, use of the
1993	ioxaglate	n = 250	40%	1,000 IU/h	Closure o.lab	18 vs 14	NS	nonionic agent rather than the ionic agent
#14	iohexol	n = 250	0%	infusion	MACE	7 vs 8	NS	emerged as an independent predictor of acute in-laboratory re-thrombosis."
Lefevre		n = 64	100%	10,000 bolus	% area of g.w.	24.1 ± 5.7% vs		"This in vivo study ... confirms that of the
1994	ioxaglate	n = 32	—		with thrombus	52.3 ± 7.0%	0.004	two low osmolality contrast media the
#15	iopamidol	n = 32	—		MACE	1 vs 2	NS	antithrombogenic effect of the ionic product is greater than that of the nonionic product."
Grines		n = 211	—	5,000–10,000 bolus,	re-catheterization	3.0% vs 11.4%	0.02	"... in patients with unstable ischemic
1996	ioxaglate	n = 106	57.4%	infusion 1,000/h	re-PTCA	1.0% vs 5.8%	NS	syndromes undergoing coronary
#16	iopamidol	n = 105	42.6%		MACE	5.8% vs 9.6%	NS	angioplasty, the use of ionic low osmolar contrast medium reduces the risk of ischemic complications ..."
Qureshi		n = 30	—	5,000–10,000 bolus	new thrombus	5 vs 11	0.028	"Nonionic low osmolality contrast medium
1997	ioxaglate	n = 15	100%		total Thrombus	25 vs 27	NS	was associated with significantly more
#17	iopamidol	n = 15	—		MACE	no data provided	?	patients developing angioscopically visible new thrombus."

(14). However, we have used a higher initial heparin-dose (20,000 IU vs 10,000 IU), and stents were implanted in 574 of 2,441 coronary lesions, while Piessens did not use intracoronary stenting at all. The incidence of abrupt closure was lower in the present study (6.5% vs 10.2%), and major ischemic events occurred less frequently (2.8% vs 3.0%). Whether these observed differences between both trials are due to clinical or technical reasons is not easy to determine. Most probably, they are attributable to the deliberate but consequent use of coronary stents in case of dissection or unsatisfactory angiographic results.

Recent data of Aguirre et al. (25) are in agreement with our findings. A meta-analysis of the 30-d composite endpoint (death, myocardial infarction, urgent re-intervention) among 5,129 patients enrolled in the EPIC, EPILOG, and CAPTURE trials receiving either nonionic or ionic contrast media revealed no difference between both types of agents (8.5% (nonionic) vs. 8.4% (ionic); $p = 0.98$). Abciximab significantly reduced event rates by a similar magnitude regardless of nonionic or ionic contrast medium use.

Limitations and possible concerns. The activated clotting time was not measured routinely in all patients. There is a patient variability in heparin response (6). In preliminary investigations carried out previously in our catheterization laboratory, we have found an activated clotting time of >350 seconds in virtually all patients receiving a bolus of 20,000 units of heparin. Since then, we have adopted this regimen as a clinical routine for several years. These observations are in agreement with data of Murkherjee et al. (26). In patients undergoing PTCA, they found complete abolition of the influence of both nonionic and ionic contrast media on thrombin generation after a bolus injection of 20,000 units of heparin. Therefore, adequacy of heparinization was presumably achieved in our patients, although activated clotting times were not monitored routinely.

Post-PTCA creatine kinase levels were measured only in symptomatic patients or when electrocardiographic changes occurred, and the patients were followed only until hospital discharge but not subsequently. Therefore, the "true" incidence of myocardial infarction may have been underestimated. On the other hand, less than 20% of our patients had unstable angina or myocardial infarction, and more than 70% of all target lesions were ACC/AHA type A and type B. The average clinical risk of our patients may have been lower than in other trials focusing on high-risk coronary interventions but may well reflect the clinical routine of high-volume institutions. Additionally, the technical factors mentioned above (heparin dose and stent implantation) also may have contributed to this comparatively low figure of ischemic complications.

Intracoronary fibrinolytics were used more frequently in the nonionic contrast medium group. Although this was not predefined as an endpoint of this study, the data require some consideration. Fibrinolytics were used before balloon inflation in eight patients in the nonionic contrast medium group, as compared with only two patients in the ionic group. This difference was apparently due to the higher incidence of intracoronary thrombus in patients allocated to receive the nonionic agent (4.2% vs 2.7%). After balloon angioplasty, six patients in the nonionic group and two patients in the ionic group were treated with fibrinolytics, and the incidence of intracoronary thrombus was 2.8% in either group. As compared with pre-PTCA, the incidence decreased by 1.4% with the nonionic contrast medium but increased by 0.1% with use of the ionic agent.

Intracoronary stents were also used more frequently in patients randomized to receive the nonionic contrast medium (31.6% vs 25.7%). They were used predominantly for treatment of dissection or an unsatisfactory angiographic result after balloon angioplasty. The incidence of dissection (30.2% vs 25.0%) as well as elastic recoil (4.6% vs 2.8%) was higher in the nonionic contrast medium group. It is, however, very unlikely that contrast media have any impact on dissections and recoil after balloon dilatation. On the other hand, the nonionic contrast medium had a higher iodine concentration (350 mg vs 320 mg). It is therefore conceivable that in the ionic contrast medium group fewer dissections were detected because of poorer opacification of the target lesion. A subgroup analysis of patients with and without intracoronary stents revealed no differences in the incidence of abrupt closure and major adverse cardiac events between both contrast medium groups. In other words, even if patients with stents would have been excluded from the analysis, contrast media was not an important factor in altering clinical events.

Conclusions. Nonionic contrast media are weaker anticoagulants than ionic compounds. Some authors have claimed even procoagulant properties, and questions have been raised as to the potential role of nonionic contrast agents in the development of acute coronary thrombosis during coronary angioplasty. The data presented here do not support this theory. No differences between the nonionic (iomeprol) and ionic contrast medium (ioxaglate) were observed with regard to angiographic and clinical endpoints. The observed in vitro differences between nonionic and ionic contrast media seem to be insignificant under clinical conditions. However, allergic side effects requiring treatment occurred only in the ionic contrast medium group. It is concluded that nonionic contrast media do not increase the risk of thrombotic complications but minimize the risk of allergic reactions in patients undergoing coronary interventions.

Reprint requests and correspondence: Prof. Dr. Rainer Schräder, Cardioangiologisches Centrum Bethanien, Im Prüfling 23, D-60389 Frankfurt, Germany.

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