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Percutaneous transluminal coronary angioplasty of left main stenosis – results of the German PTCA registry

Perkutane transluminale Koronarangioplastie – Ergebnisse des Deutschen PTCA-Registers

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Zusammenfassung Die Behandlung hochgradiger symptomatischer Hauptstammstenosen der linken Koronararterie ist die operative Revaskularisation. Bei geschütztem Hauptstamm durch vorangegangene Bypass-Operation oder als Notfall-Eingriff im akuten Myokardinfarkt mit kardiogenem Schock wird die perkutane transluminale Angioplastie als Behandlungsalternative durchgeführt. Die Durchsicht von 262 Interventionen ergab eine Mortalität der Intervention von 9,1% (4/44) bei Patienten ohne Hauptstamm-Protektion, 4,8% (1/21) bei Patienten mit Kollateralen und 0,5% (1/197) bei Patienten mit offenem Bypass-Gefäß zu einem der Gefäße der linken Koronararterie. Die koronare Angioplastie des ungeschützten Hauptstamms hat ein nicht akzeptables Risiko und sollte daher auch als Notfall-Eingriff nicht durchgeführt werden. Das Risiko der Hauptstamm-PTCA kann durch die vorgeschlagene Einteilung der Hauptstamm-Protektion durchgeführt werden.

Schlüsselwörter PTCA – linker Hauptstamm – Angioplastie

Summary In cases with protected left main stenosis by previous bypass surgery or as an emergency intervention in patients presenting with acute myocardial infarction and cardiogenic shock, percutaneous transluminal coronary angioplasty is performed as an alternative treatment strategy to bypass surgery. A review of 262 left main angioplasties revealed a procedure-related mortality in cases without protection of the left main coronary artery of 9.1% (4/44), in cases with partially protected left main stenosis by collaterals to either left coronary artery of 4.8% (1/21) and 0.5% (1/187) in cases with nonobstructed bypass grafts to either left coronary artery. Coronary angioplasty of an unprotected left main coronary artery, had an unacceptably high procedure-related mortality rate and should therefore not be performed even in cases of emergency intervention. The risk stratification of the procedure can be evaluated by the proposed grading of left main artery protection.

Key words PTCA – left main coronary artery – angioplasty

Introduction

According to the American Heart Association/American College of Cardiology (AHA/ACC) Guidelines coronary angioplasty is absolutely contraindicated if “there is a significant obstruction (>50%) in the left main coronary artery and this main segment is not protected by at least one nonobstructed bypass graft to the left anterior descending or left circumflex artery” (12). The long-term experiences of the Coronary Artery Surgery Study (CASS) Registry (12) and the Coronary Artery Bypass Graft Surgery Trialists Collaboration (17) showed the superiority of surgical treatment as compared to medical treatment concerning the overall mortality. Despite these guidelines and study results, advances in operator experience, improvements of angioplasty technique and new angioplasty devices have extended the indication of coronary angioplasty even to left main coronary artery stenosis (7, 8). The aim of the current investigation was to determine the in-hospital outcome of patients undergoing left main angioplasty in the PTCA registry of the “Arbeitsgemeinschaft Leitender Kardiologischer Krankenhausärzte (ALKK)” study group.

Methods

The previously described PTCA registry of German community hospitals represents approximately one third of all angioplasty procedures performed in Germany (16). Each angioplasty procedure was included on an intention-to-treat basis. The procedures registered as left main angioplasty were reviewed together with data concerning the in-hospital outcome in a core laboratory in Detmold, Germany. The review of all angiograms was performed by two senior cardiologists blinded to the procedural and the in-hospital outcome unless the course of the patient could be gathered from the angiography.

Definitions

Left main protection was graded as the following: *unprotected* left main stenosis without collateral flow or open bypass grafts to the left anterior descending or to the left circumflex artery, *partially protected* left main stenosis with collateral flow to the left anterior descending or to the left circumflex artery, and *protected* left main stenosis with nonobstructed bypass vessels to the left anterior descending or left circumflex artery.

Left ventricular function was classified as normal (ejection fraction >65%), mildly impaired (ejection fraction 45–65%), or severely impaired (ejection fraction <45%). Classification of cause of death was done

as an integrated assessment of the coronary angiography, reports of the procedure and the clinical course. Procedure-related death was defined as normal blood flow (thrombolysis in myocardial infarction grade 3) in both left coronary arteries with normal ventricular excursions before the start of the intervention or compromised blood flow (thrombolysis in myocardial infarction grade <3) in either left coronary artery with depressed heart excursions after the intervention. Death despite PTCA was defined as technically successful intervention and lethal outcome. Start of the intervention was defined as passage of the left main stenosis with the guide wire.

Statistical methods

Data are reported as mean±standard deviation (SD). Continuous variables were compared by using Student's t-test for independent samples. The Wilcoxon test was used for categorical variables. A Chi-square test or Fischer's exact test (for cells <5) was used to determine the 2-tailed statistical significance of associations in 2-by-2 tables. Different variables were tested for independent correlation with death by multiple regression analysis. P values <0.05 were considered to indicate statistical significance. Data management and analysis were performed by the STATISTICA for Windows software package release 5.0 (StatSoft, Inc. Tulsa).

Results

Between October 1992 and September 1997, 580 prospectively announced angioplasty procedures were registered as left main angioplasties in 68 German community hospitals organized in the ALKK (Arbeitsgemeinschaft Leitender Kardiologischer Krankenhausärzte) study group.

Angiography, procedural and clinical outcome of all 580 procedures were requested for evaluation in a core laboratory in Detmold, Germany 320 (55%) complete procedures were made available for evaluation. Of these, 58 (18%) were interventions of proximal left anterior descending or proximal left circumflex arteries. The remaining 262 procedures were either angioplasty of protected left main stenosis or emergency left main interventions in patients with an acute myocardial infarction or cardiogenic shock. The data of these 262 procedures were compared to 141 454 non-left main angioplasty procedures.

Baseline data and angiographic characteristics are shown in Table 1. Patients in the left main PTCA group were older and had more often three-vessel disease as compared with the non-left main patient cohort. The

Table 1 Baseline characteristics

	PTCA registry (n=141 454)	Left-main PTCA (n=262)
Age [years±SD]	61.6±10	65.2±9
Male sex	109 061 (77.1%)	220 (84%)
Coronary heart disease:		
one-vessel	66 625 (47.1%)	0
two-vessel	48 660 (34.4%)	64 (24.5%)
multivessel	26 169 (18.5%)	198 (75.5%)
Left ventricular function:		
normal	83 741 (59.2%)	77 (29.4%)
mildly impaired	50 640 (35.8%)	80 (30.5%)
severely impaired	7 073 (5%)	31 (11.8%)
LV angiogram not available	0	74 (28.3%)
Indication for intervention:		
stable angina	79 497 (56.2%)	130 (49.5%)
unstable angina	33 242 (23.5%)	70 (26.7%)
acute myocardial infarction	14 570 (10.3%)	48 (18.3%)
other	14 145 (10%)	14 (5.5%)
AHA/ACC stenosis type:		
A	18 955 (13.4%)	24 (9.2%)
B1	46 680 (33%)	77 (29.4%)
B2	52 479 (37.1%)	103 (39.3%)
C1	14 711 (10.4%)	33 (12.6%)
C2	8 629 (6.1%)	25 (9.5%)

Table 2 Clinical outcome of all patients

	Left-main PTCA (n=262)	PTCA registry (n=141 454)	p value
Myocardial infarction*	6/218 (2.8%)	2222 (1.6%)	0.35
CK max	1334 U/l (mean)	549 U/l (mean)	–
Urgent CABG	2 (0.76%)	338 (0.24%)	0.08
Procedure-related death	6 (2.3%)	571 (0.4%)	<0.001
Death despite PTCA	27 (10.3%)	729 (0.52%)	<0.001
Non-cardiac death	2 (0.79%)	57 (0.04%)	<0.001

*Patients with acute myocardial infarction at the time of PTCA are excluded

distribution of the stenosis type according to the AHA/ACC guidelines was similar in both groups. Left ventricular function was more frequently impaired in the left main PTCA group. In 28.3%, left ventricular angiography was not performed because of cardiogenic shock.

The overall procedure-related mortality is summarized in Table 2. The degree of left main protection influenced clinical outcome as follows: the procedure-related mortality in patients without any left main protection was 9.1% (Table 3), in patients with collaterals 4.8% (Table 4) and 0.5% (Table 5) with open bypass grafts to either left coronary artery whereas the procedural mortality of the non-left main angioplasty cohort was 0.4%.

There was also a difference in procedure-related mortality depending on the indication for angioplasty of

Table 3 Clinical outcome of all patients with unprotected left main

	Unprotected left-main PTCA (n=44)	PTCA registry (n=141 454)	p value
Myocardial infarction*	4 (9.1%)	2222 (1.6%)	<0.001
CK max	3250 U/l (mean)	549 U/l (mean)	–
Urgent CABG	1 (2.3%)	338 (0.24%)	0.006
Procedure-related death	4 (9.1%)	571 (0.4%)	<0.001
Death despite PTCA	23 (52.3%)	729 (0.52%)	<0.001
Non-cardiac death	1 (2.3%)	57 (0.04%)	<0.001

* See Table 2

Table 4 Clinical outcome in patients with partially protected left main

	Partially protect left-main PTCA (n=21)	PTCA registry (n=141 454)	p value
Myocardial infarction*	1 (4.8%)	2222 (1.6%)	0.24
CK max	195 U/l (mean)	549 U/l (mean)	–
Urgent CABG	1 (4.8%)	338 (0.24%)	<0.001
Procedure-related death	1 (4.8%)	571 (0.4%)	0.002
Death despite PTCA	3 (14.3%)	729 (0.52%)	<0.001
Non-cardiac death	0	57 (0.04%)	0.89

* See Table 2

Table 5 Clinical outcome in patients with protected left main

	Protected left-main PTCA (n=197)	PTCA registry (n=141 454)	p value
Myocardial infarction*	1 (0.5%)	2222 (1.6%)	0.23
CK max	438 U/l (mean)	549 U/l (mean)	–
Urgent CABG	0	338 (0.24%)	0.49
Procedure-related death	1 (0.5%)	571 (0.4%)	0.89
Death despite PTCA	1 (0.5%)	729 (0.52%)	0.99
Non-cardiac death	1 (0.5%)	57 (0.04%)	<0.001

* See Table 2

the left main (Table 6). Patients who underwent left main angioplasty for stable angina had a lower mortality as compared with those with unstable angina (Table 6). The highest mortality was found in patients presenting with acute myocardial infarction (Table 6). One patient died because of fulminant pulmonary embolism two weeks after the procedure; one patient died from a carcinoma of the pancreas six months later.

The multivariate regression analysis identified the degree of left main protection ($p<0.001$), indication for angioplasty ($p<0.001$) and left ventricular function ($p=0.002$) as independent predictors for procedure-related mortality.

Table 6 Clinical outcome dependent on the indication for angioplasty

Indication	Procedure-related death	Death despite PTCA	Non-cardiac death
Stable angina	0	1/129 (0.8%)	1/129 (0.8%)
Unstable angina	2/70 (2.9%)	1/70 (1.4%)	0
Acute myocardial infarction	4/48 (8.3%)	31/48 (64.6%)	1/48 (2.1%)
Prognostic indication	0/15	0/15	0/15

* See Table 2

Discussion

An angiographically proven stenosis of the left main coronary artery without protection by a nonobstructed bypass graft is considered to be a contraindication for coronary angioplasty (12). Coronary artery bypass surgery has been shown to improve survival of patients with left main stenosis (1, 17), although these patients represent the highest risk group for bypass surgery with an overall operative mortality of 3.5% (2). Technical improvement and the development of coronary artery stents (3, 6, 14, 15) enable interventional cardiologists to treat even complex coronary lesions, so that in specific conditions coronary angioplasty of protected or even unprotected left main stenosis has been performed.

Laruelle et al. reported in a small series of elective angioplasty in patients with an unprotected left main stenosis a procedural mortality of 7.7% and a rate of myocardial infarction of 2.8% without stent implantation. Because of the high mortality rate the following ten patients of this study underwent elective stent implantation and had no serious adverse events during the hospital phase (7). Major in-hospital complications also did not occur in the study of Park et al. performing elective stent implantation in selected patients (11). The results of these two single center studies could not be confirmed either by the multicenter registry analysis by Ellis and coworkers reporting a procedural mortality of 5.9% with (n=51) and without (n=68) stenting (4) or by the results of the present study reporting a procedural mortality of 9.1% in unprotected left main stenosis. However, these investigations have limited comparability because the patients in the studies of Laruelle et al. and Park et al. are highly selected with normal left ventricular function whereas the patients in the multicenter registry analysis of Ellis et al. were not selected and in the present study the patients who had an unprotected left main stenosis all presented with acute myocardial infarction. Despite these differences in the study population a 0% mortality in interventional cardiology can only be a problem of a small study cohort and does not seem realistic.

Considering the patient characteristics, the poor outcome of this highest risk group was not unexpected. Even in cases presenting with acute myocardial infarction and cardiogenic shock the intervention seems to be problematic. Mortality is per se high in these patients (52.3%) and is burdened by an additional procedure-related mortality of 9.1%. The question arises whether further lives could have been saved by avoiding coronary interventions and by transferring such patients to emergency bypass surgery.

Patients with partially protected left main stenosis who underwent coronary angioplasty had a lower mortality compared to those without any left main protection, but had a significantly higher incidence of major in-hospital events as compared with the non-left main angioplasty cohort (Table 4).

With our registry data it could be demonstrated that patients with open bypass grafts to either left coronary artery undergoing left main angioplasty had a comparable procedure-related and in-hospital mortality as compared to the non-left main angioplasty cohort. These findings are in accordance with the largest published series by O'Keefe et al. reporting a high survival rate (90% at 3 years) after angioplasty of 127 protected and unprotected left main coronary arteries (10).

Several criteria are proposed to select the suitable patient for these interventional procedures (11) because development of easily applicable stent models and improvement in the stent implantation technique (3) with a modified anticoagulation regimen (13) led to a lack of respect for coronary angioplasty among interventional cardiologists especially in cases with complex lesion morphology (9). Multiple regression analysis of our data identified left main protection, indication for angioplasty and left ventricular function as independent predictors for procedure-related mortality. The classification of the degree of left main protection combined with left ventricular function represents an easily applicable grading system for risk stratification of interventions in patients with symptomatic left main stenosis.

Study limitations

National guidelines prohibit coronary intervention in patients with unprotected left main stenosis (5, 12); therefore a randomization between coronary angioplasty and bypass surgery is not feasible. The study population in the present multicenter registry analysis consists of emergency patients and elective patients with protected left main stenosis.

The analysis included only 54.8% of all procedures prospectively classified as interventions of left main stenosis. It seems highly unlikely that a potential selection bias led to a higher mortality rate than present in

the whole cohort of left main angioplasties. The opposite is probably true and would therefore underline the conclusions reached.

Conclusions and clinical implications

Patients with symptomatic stenosis of the left main coronary artery and nonobstructed bypass vessels to either left coronary artery may be treated by coronary intervention with a procedure-related mortality and incidence of myocardial application comparable to that of

the non-left main angioplasty cohort. Patients with unprotected symptomatic left main stenosis should preferably be transferred to emergency cardiac surgery, because the high procedural mortality discourages percutaneous cardiac interventions. Even in cases presenting with acute myocardial infarction characterized by a high primary mortality, coronary interventions should be avoided.

Furthermore, in our opinion treatment indications that are not in accordance with guidelines of several national committees should not be based on single center experiences and small study cohorts.

References

- Caracciolo EA, Davis KB, Sopko G, Kaiser GC, Corley SD, Schaff H, Taylor HA, Chaitman BR, for the CASS Investigators (1995) Comparison of surgical and medical group survival in patients with left main coronary artery disease. *Circulation* 91:2325–2334
- Chairman BR, Fisher LD, Bourassa MG (1981) Effects of coronary bypass surgery on survival patterns in patients with left main coronary artery disease. Report of the Collaborative Study in Coronary Artery Surgery (CASS). *Am J Cardiol* 48:765–777
- Colombo A, Hall P, Nakamura S, Almagor Y, Maiello L, Martini G, Gaglione A, Goldberg SL, Tobis JM (1995) Intracoronary stenting without anticoagulation accomplished with intravascular ultrasound guidance. *Circulation* 91:1676–1688
- Ellis SG, Tamai H, Nobuyoshi M, Kosuga K, Colombo A, Holmes DR, Macaya C, Grines CL, Whitlow PL, White HJ, Moses J, Teirstein PS, Serruys PW, Bittl JA, Mooney MR, Shimshak TM, Block PC, Erbel R (1997) Contemporary percutaneous treatment of unprotected left main coronary stenoses: initial results from a multicenter registry analysis 1994–1996. *Circulation* 96:3867–3872
- Erbel R, Engel HJ, Kübler W, Meinertz T, Neuhaus KL, Sauer G, Strauer BE, Bonzel T, Ewen K (1997) Richtlinien der interventionellen Koronartherapie. *Z Kardiol* 86:1040–1063
- Fischman DL, Leon MB, Baim DS, Schatz RA, Savage MP, Penn I, Detre K, Veltri L, Ricci D, Nobuyoshi M, Cleman M, Heuser R, Almond D, Teirstein PS, Fish D, Colombo A, Brinker J, Moses J, Shaknovich Hirshfeld J, Bailey S, Ellis S, Rake R, Goldberg S (1994) For the Stent Restenosis Study Investigators. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. *N Engl J Med* 331:496–501
- Laruelle CJJ, Brueren GBR, Ernst SMPG, Bal ET, Mast GE, Suttorp M-J, Burtel de la Riviere A, Plokker THW (1998) Stenting of “unprotected” left main coronary artery stenosis: early and late results. *Heart* 79:148–152
- Lopez JJ, Ho KKL, Stoler RC, Caputo RP, Carozza JP, Kuntz RE, Baim DS (1997) Percutaneous treatment of protected and unprotected left main coronary stenosis with new devices: immediate angiographic results and intermediate-term follow-up. *J Am Cardiol* 29:345–352
- Miketic S, Carlsson J, Tebbe U (1997) Safety and efficacy of angiographic guided elective Palmaz-Schatz™ stent implantation without coumadin: comparison of stent implantation and angioplasty. *J Interven Cardiol* 10:265–270
- O’Keefe JH Jr, Hartzler GO, Rutherford BD, McConahay DR, Johnson WL, Giorgi LV, Ligon RW (1989) Left main coronary angioplasty: early and late results of 127 acute and elective procedures. *Am J Cardiol* 64:144–147
- Park SJ, Park SW, Hong MK, Cheong SS, Lee CW, Kim JJ, Hong MK, Mintz GS, Leon MB (1998) Stenting of unprotected left main coronary artery stenoses: immediate and late outcomes. *J Am Coll Cardiol* 3:37–42
- Ryan TJ, Baumann WB, Kennedy JW, Kereiakes DJ, King III SB, McCallister BD, Smith SC, Ulluyot DJ (1993) Guidelines for percutaneous transluminal coronary angioplasty. *Circulation* 88:2987–3006
- Schömig A, Neumann F-J, Kastrati A, Schühlen H, Blasini R, Hadamitzky M, Walter H, Zitzmann-Roth E-M, Richardt G, Alt E, Schmitt C, Ulm K (1996) A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary-artery stents. *N Engl J Med* 334:1084–1089
- Serruys PW, de Jaegere P, Kiemeneij F, Macaya C, Rutsch W, Heyndrickx G, Emanuelsson H, Marco J, Legrand J, Materne P, Belardi J, Sigward U, Colombo A, Goy JJ, van den Heuvel P, Delcan J, Morel MA for the Benestent Study Group (1994) A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coronary artery disease. *N Engl J Med* 331:489–495
- Topol EJ (1994) Daveats about elective coronary stenting. *N Engl J Med* 331:539–541
- Vogt A, Bonzel T, Harmjan D, v. Leitner E-R, Pfafferot C, Engel H-J, Niederer W, Schuster P-R, Glunz HG, Neuhaus K-L for the Arbeitsgemeinschaft Leitender Kardiologischer Krankenhausärzte (ALKK)-study group. PTCA registry of German Community hospitals. *Eur Heart J* 1007; 18:1110–1114
- Yusuf S, Zuckere D, Peduzzi P, Fisher LD, Takaro T, Kennedy JW, Davis K, Killip T, Passamani E, Norris R, Morris C, Mathur V, Varnauskas E, Chalmers TC (1994) Effect of coronary artery bypass graft surgery on survival: overview of 10-years result from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet* 344:563–570