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Smokers *versus* non-smokers undergoing percutaneous transluminal coronary angioplasty: The impact of clinical and procedural characteristics on in-hospital mortality

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Abstract

Background: *We aimed to compare clinical and procedural characteristics of unselected smokers and non-smokers undergoing percutaneous transluminal coronary angioplasty (PTCA) and to assess their impact on in-hospital mortality.*

Methods: *One thousand consecutive patients treated interventionally were retrospectively enrolled into a single academic centre registry.*

Results: *Smokers (n = 631), in comparison to non-smokers (n = 369), were younger and less likely to be hypertensive, diabetic and female gender. History of myocardial infarction and pre-existing heart failure were also less frequent in the group of smokers. Furthermore, univariate analysis revealed more frequent presentation with acute coronary syndromes (ACS), shorter overall duration of PTCA, shorter exposure to X-rays and lower volume of contrast medium administered in smokers than in non-smokers. Conversely, non-smokers were characterized by considerably higher prevalence of multivessel disease, lower completeness of revascularization and worse final epicardial flow in primary PTCA procedures. Moreover, non-smokers experienced higher crude in-hospital mortality than smokers in the setting of unstable angina/non-ST-segment elevation myocardial infarction (0.0%* vs. *6.0%, p = 0.0544) and ST-segment elevation myocardial infarction (6.0%* vs. *14.0%, p < 0.02). Smoking status, when adjusted for the baseline characteristics, did not possess any predictive value in terms of in-hospital mortality and surrogates of intervention complexity.*

Conclusions: *A strong trend towards decreased mortality among smokers undergoing PTCA was observed when compared to non-smokers. However, the survival advantage might be fully explained by the younger age of the smokers, their more favourable clinical characteristics and less extensive coronary atherosclerosis.* (Cardiol J 2007; 14: 482–492)

Key words: percutaneous transluminal coronary angioplasty, smoking, in-hospital mortality, comorbidities

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Introduction

Coronary artery disease (CAD) imposes a significant health burden and remains a life-threatening condition. Hence, both its prevention and treatment are considered as priorities.

Percutaneous transluminal coronary angioplasty (PTCA) in comparison with optimal pharmacotherapy has been proven to reduce mortality and incidences of subsequent cardiovascular events in patients treated for myocardial infarction and unstable angina [1, 2] and to improve quality of life in stable angina subjects [3]. The number of percutaneous coronary interventions has increased dramatically in recent years, with more than 650,000 such procedures now performed annually in the United States [4]. With the advent of new generations of stents, it is supposed that even more percutaneous interventions will be performed as they replace a substantial proportion of coronary bypass procedures.

Smoking has been identified as a strong risk factor for premature coronary atherosclerosis, atherothrombotic events and sudden cardiac death [5, 6]. Smoking was demonstrated to induce a hypercoagulability state and to promote low-grade inflammation [7] as well as to release catecholamines that exert pro-arrhythmogenic effects [8] and lead to an increase of both heart rate and arterial blood pressure [9]. In addition, exposure to tobacco smoke triggers coronary artery vasoconstriction [10] and reduces oxygen supply due to elevated carbon monoxide levels [11]. Nevertheless, thrombolytic trials reported lower short-term mortality rates among smokers suffering from myocardial infarction [12–15].

The aim of the study was to compare clinical and procedural characteristics of smokers and non-smokers undergoing PTCA due to symptomatic CAD and to assess their impact on in-hospital mortality.

Methods

Study design and patients

One thousand consecutive patients were retrospectively enrolled into a single academic centre registry. All subjects were admitted to the Department of Cardiology and Internal Medicine of the University Hospital in Bydgoszcz between June 2002 and April 2003 for interventional treatment of symptomatic CAD. Study participants were interviewed to obtain a detailed medical history (with a special emphasis on comorbidities and risk factors for CAD) and underwent a physical examination. The patients' invasive treatment charts and their angiographic recordings were analysed. According to self-reported smoking status, participants were categorized as smokers (631 patients) or non-smokers (369 patients). The group of smokers included current smokers (297 subjects) and former smokers (334 subjects).

Depending on the clinical status of the patients, PTCA was performed in 3 modes: elective — for stable angina (SA) patients (n = 492; 49.2%); urgent — for unstable angina (UA)/non-ST-segment elevation myocardial infarction (NSTEMI) patients (n = 164; 16.4%) and emergency — for ST-segment elevation myocardial infarction (STEMI) patients (n = 344; 34.4%).

The inclusion criterion was the presence of significant (> 50% of artery diameter) stenosis in ≥ 1 clinically relevant (> 1.5 mm in diameter) coronary artery supplying viable ischemic myocardial tissue. Patients with significant stenosis of the left main trunk were excluded from the study. All intervention was carried out in compliance with standard guidelines using a Toshiba CAS-10A angiography device. Each PTCA procedure was preceded by an angiographic study. Bare metal stents were implanted at the operator's discretion. Combined final TIMI flow 2 or 3 in the dilated vessel and residual stenosis not exceeding 20% of the referential diameter was regarded as an effective procedure. Complete revascularization was accomplished when all clinically relevant lesions (defined above) were treated. In each case, written informed consent for coronary angioplasty was required. The study protocol was approved by the local ethics committee.

Demographic and clinical characteristics of the study population as well as distribution of selected angiographic and procedural features in the compared groups are displayed in Tables 1 and 2, respectively.

Patient management depended on the mode of qualification for the invasive procedure. Elective interventions were preceded by oral administration of aspirin (75–150 mg once daily) to all patients and additional administration of ticlopidine (250 mg twice daily) at least 72 hours prior to PTCA. Patients qualifying for urgent/emergency procedure were pretreated with a 300 mg loading dose of clopidogrel. Independently of the mode of management unless contraindicated, each patient was given unfractionated heparin intravenously (100 IU/kg) and an intracoronary bolus of nitroglycerin (0.3 mg) directly prior to the procedure. Only iso-osmolar or

Table 1. Demographic and clinical characteristics of the analysed groups.

Parameters	Current smokers (n = 297)	Former smokers (n = 334)	Non--smokers (n = 369)	p between current smokers and non--smokers	p between former smokers and non--smokers	p between ever smokers and non--smokers
Age (years)	55.2 ± 10.2	59.4 ± 9.5	64.6 ± 10.8	< 0.000001	< 0.000001	< 0.000001
Male gender	236 (79.5%)	269 (80.5%)	196 (53.1%)	< 0.0001	< 0.0001	< 0.0001
Indications for PTCA:						
SA	80 (26.9%)	216 (64.7%)	196 (52.1%)			
UA/NSTEMI	37 (12.5%)	47 (14.1%)	80 (14.1%)	< 0.0001	< 0.005	< 0.0001
STEMI	180 (60.6%)	71 (21.2%)	93 (33.8%)			
Cardiogenic shock	17 (5.7%)	7 (2.1%)	17 (4.6%)	NS	0.067	NS
History of MI	85 (28.6%)	187 (56.0%)	182 (49.3%)	< 0.0001	0.0772	0.0568
Chronic heart failure	28 (9.4%)	47 (14.1%)	70 (19.0%)	< 0.0007	0.0816	< 0.03
History of stroke	13 (4.4%)	20 (6.0%)	22 (6.0%)	NS	NS	NS
PAD	24 (8.1%)	29 (8.7%)	13 (3.5%)	< 0.02	< 0.004	< 0.003
Hypertension	151 (50.8%)	199 (59.6%)	256 (69.4%)	< 0.0001	< 0.007	< 0.0001
Diabetes mellitus	24 (8.1%)	61 (18.3%)	107 (29.0%)	< 0.0001	< 0.001	< 0.0001
BMI [kg/m^2]	26.9 ± ?3.8	27.4 ± 3.5	27.8 ± 4.0	< 0.009	NS	< 0.05
Hypercholesterolemia	235 (79.1%)	286 (85.6%)	287 (77.8%)	NS	< 0.008	0.0635
Family history of CAD	83 (27.9%)	111 (33.2%)	84 (22.8%)	NS	< 0.003	< 0.007

PAD — peripheral arterial disease; PTCA — percutaneous transluminal coronary angioplasty; MI — myocardial infarction; BMI — body mass index; CAD — coronary artery disease; SA — stable angina; UA — unstable angina; STEMI — ST-segment elevation myocardial infarction; NSTEMI — non--ST-segment elevation myocardial infarction

Table 2. Angiographic and procedural characteristics of the analysed groups.

Parameters	Current smokers (n = 297)	Former smokers (n = 334)	Non--smokers (n = 369)	p between current smokers and non--smokers	p between former smokers and non--smokers	p between ever smokers and non--smokers
Coronary artery disease:						
single-vessel	128 (43.1%)	100 (29.9%)	94 (25.5%)	< 0.0001	NS	< 0.0006
multivessel	169 (56.9%)	234 (70.1%)	275 (74.5%)			
Localization of culprit lesion:						
right coronary artery	124 (41.7%)	111 (33.2%)	136 (36.9%)			
left coronary artery	171 (57.6%)	219 (65.6%)	230 (62.3%)			
saphenous venous graft	2 (0.7%)	4 (1.2%)	2 (0.5%)	NS*	NS*	NS*
left internal mammary artery	0 (0%)	0 (0%)	1 (0.3%)			
Restenosis as a reason for PTCA	5 (1.7%)	15 (4.5%)	16 (4.3%)	0.0515	NS	NS
Baseline blood flow in the culprit vessel:						
TIMI 0 or 1	148 (49.8%)	100 (29.9%)	112 (30.4%)	< 0.0001	NS	< 0.005
TIMI 2 or 3	149 (50.2%)	234 (70.1%)	257 (69.6%)			
Baseline blood flow in the culprit vessel exclusively in STEMI patients:						
TIMI 0 or 1	123 (68.3%)	53 (74.6%)	66 (71.0%)	NS	NS	NS
TIMI 2 or 3	57 (31.7%)	18 (25.4%)	27 (29.0%)			

cont.→

Table 2. cont. Angiographic and procedural characteristics of the analysed groups.

Parameters	Current smokers (n = 297)	Former smokers (n = 334)	Non--smokers (n = 369)	p between current smokers and non--smokers	p between former smokers and non--smokers	p between ever smokers and non--smokers
Final blood flow in the culprit vessel:						
TIMI 0 or 1	19 (6.4%)	20 (6.0%)	24 (6.5%)	NS	NS	NS
TIMI 2 or 3	278 (93.6%)	314 (94.0%)	345 (93.5%)			
Final blood flow in the culprit vessel exclusively in STEMI patients:						
TIMI 0 or 1	9 (5.0%)	7 (9.9%)	11 (11.8%)	< 0.05	NS	0.095
TIMI 2 or 3	171 (95.0%)	64 (90.1%)	82 (88.2%)			
Usage of abciximab	88 (29.6%)	44 (13.2%)	54 (14.6%)	< 0.0001	NS	< 0.02
Recanalization of chronic total occlusion	35 (11.8%)	32 (9.6%)	41 (11.1%)	NS	NS	NS
Multivessel PTCA	8 (2.7%)	10 (3.0%)	11 (3.0%)	NS	NS	NS
Applied PTCA method:						
POBA	36 (12.1%)	71 (21.3%)	71 (19.2%)	< 0.02	NS	NS
stenting	261 (87.9%)	263 (78.7%)	298 (80.8%)			
Direct stenting	100 (33.7%)	82 (24.5%)	89 (24.1%)	< 0.007	NS	NS
Maximal stent or balloon length [mm]	17.3 ± 5.4	17.5 ± 5.8	17.4 ± 5.6	NS	NS	NS
Maximal stent or balloon diameter [mm]	3.1 ± 0.5	3.0 ± 0.5	3.0 ± 0.5	< 0.002	NS	< 0.05
Maximal inflation pressure [atm]	13.6 ± 3.3	13.6 ± 3.3	13.3 ± 3.4	NS	NS	NS
Number of used balloons	1.0 ± 0.8	1.0 ± 0.8	1.1 ± 0.8	NS	NS	NS
Number of implanted stents	1.1 ± 0.6	0.9 ± 0.6	1.0 ± 0.7	NS	NS	NS
Duration of PTCA [min]	36.0 ± 20.7	39.0 ± 18.0	41.6 ± 22.3	< 0.00008	NS	< 0.004
X-ray exposure time [min]	8.9 ± 6.4	10.1 ± 6.2	10.6 ± 6.8	< 0.00002	NS	< 0.003
Volume of dye used [ml]	144.9 ± 80.1	150.1 ± 69.6	158.7 ± 83.4	< 0.02	NS	0.057
Angiographic outcome of PTCA:						
effective	279 (93.9%)	310 (92.8%)	342 (93.2%)	NS	NS	NS
ineffective	18 (6.1%)	24 (7.2%)	27 (6.8%)			
Revascularization:						
complete	113 (38.0%)	84 (25.1%)	74 (20.1%)	< 0.0001	NS	< 0.0002
incomplete	184 (62.0%)	250 (74.9%)	295 (79.9%)			
Qualification for further treatment:						
conservative	249 (83.8%)	271 (81.1%)	303 (82.1%)	NS	NS	NS
PTCA	43 (14.5%)	55 (16.5%)	57 (15.4%)			
CABG	5 (1.7%)	8 (2.4%)	9 (2.4%)			

*Saphenous venous grafts and left internal mammary arteries were analysed as one group; PTCA — percutaneous transluminal coronary angioplasty; STEMI — ST-segment elevation myocardial infarction; CABG — coronary artery bypass grafting; POBA — plain old balloon angioplasty

low-osmolar non-ionic contrast media were used. After stent implantation each patient received aspirin (75 mg once daily) indefinitely and ticlopidine (250 mg twice daily) for 4 weeks. Other medications were given when indicated by international recommendations [16–18].

Statistical analysis

Quantitative and qualitative data were respectively reported as arithmetical mean ± standard deviation and the sum and percentage of patients within the analysed group, presenting with a particular feature. Arithmetical means and percentage values were rounded off to one decimal place and odd ratio values to two decimal places. Examination of normal distribution of quantitative variables was performed using the Shapiro-Wilk test. Continuous variables showing normal distribution were compared with the t-test for the difference between two means of independent variables. The Mann-Whitney test was applied to compare variables which did not show Gaussian distribution. Independent prognostic factors of the short-term outcome were determined with the logistic regression model. Relations between the investigated variables and the likelihood of in-hospital mortality were estimated with the use of odds ratios (OR) and their 95% confidence intervals (95% CI). A multiple regression model was used to evaluate the independent impact of multiple variables on a continuous variable. Qualitative data were analysed and compared using the χ^2 test (applying Yeats' correction when indicated) or using the Fisher exact test. A value of $p < 0.05$ was considered statistically significant; $0.05 \leq p < 0.1$ was regarded as a trend towards statistical significance, while $p \geq 0.1$ was marked as NS. All computations were carried out with Statistica, version 7.1 (StatSoft, Tulsa, USA).

Results

Patient and procedure characteristics

Smokers, when compared to non-smokers, were referred for PTCA at a younger age (detailed comparisons with respect to clinical presentation: SA 56.7 ± 9.0 years *vs*. 61.9 ± 9.6 years, $p < 0.000001$; UA/NSTEMI 59.2 ± 11.8 years *vs*. 66.0 ± 10.9 years, $p < 0.0003$; STEMI 57.7 ± 10.5 years *vs*. 69.1 ± 11.3 years, $p < 0.000001$). An average smoker in our cohort experienced his/her first STEMI almost 13 years earlier than a non-smoker (57.0 ± 10.0 years *vs*. 69.7 ± 11.7 years, $p < 0.000001$). However, as indicated in Table 1, smokers were less likely to be hypertensive, obese, diabetic and female as well as to have less frequent history of myocardial infarction and chronic heart failure. Furthermore, univariate analysis revealed more frequent presentation with acute coronary syndromes and higher frequency of both family history of CAD and peripheral arterial disease in smokers than in non-smokers. Despite a tendency towards more frequent detection of hypercholesterolemia in smokers, rates of declared prior statin therapy were comparable in both groups. Smoking and non-smoking subjects did not differ significantly in terms of culprit lesion localization, baseline TIMI flow in the culprit vessel corrected for the clinical presentation or occurrence of cardiogenic shock (Table 2). PTCA in non-smokers was associated with longer overall duration, longer exposure to X-rays and higher volume of injected contrast medium, despite similar distributions of multivessel PTCA, recanalization of chronic total occlusions, stent application, direct stenting and the number of used balloons in the compared populations. Non-smokers were also characterized by a higher prevalence of multivessel coronary disease and lower diameter of reference vessel. On the other hand, abciximab was more frequently administered in smokers.

The angiographic efficacy of intervention measured as a proportion of patients with final TIMI 2 or 3 flow in the culprit vessel was high in both groups, without any significant differences. However, a lower completeness of revascularization and a tendency towards worse final epicardial flow in the setting of STEMI were observed in non-smokers.

In-hospital mortality and duration of hospitalisation

We noted an unadjusted in-hospital mortality rate of 2.4% in smokers compared with 4.6% in non-smokers ($p = 0.0532$). A subgroup analysis of in-hospital mortality with respect to the indication for PTCA revealed elevated mortality rates among non-smokers after interventions carried out for STEMI and UA/NSTEMI (Fig. 1). A detailed comparison of patients treated for STEMI demonstrated significant-

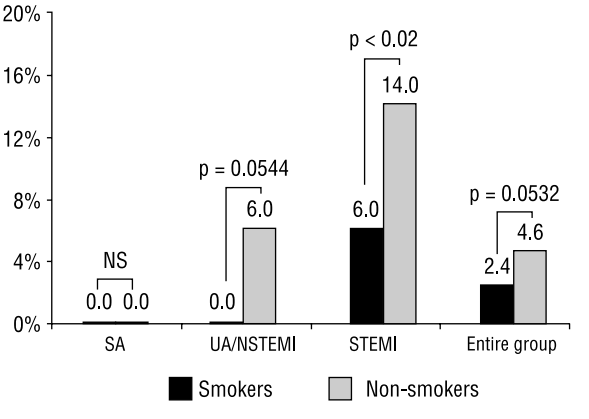

Figure 1. Comparison of in-hospital mortality rates; SA — stable angina; UA — unstable angina; STEMI — ST-segment elevation myocardial infarction; NSTEMI — non-ST-segment elevation myocardial infarction.

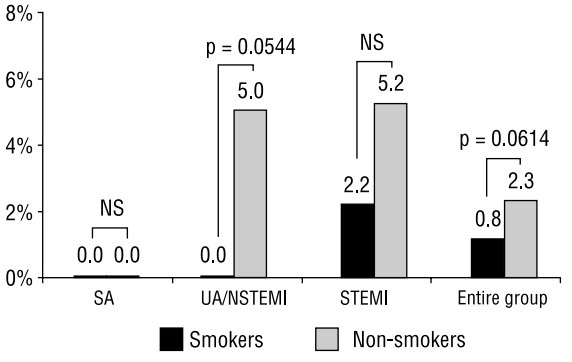

Figure 2. Comparison of in-hospital mortality rates after exeluding patients with cardiogenic shock; SA — stable angina; UA — unstable angina; STEMI — ST-segment elevation myocardial infarction; NSTEMI — non-ST-segment elevation myocardial infarction.

ly lower in-hospital mortality in current smokers than in non-smokers (4.4% *vs*. 14.0%, p < 0.006). Mortality rates did not differ significantly between former smokers and non-smokers (9.9% *vs*. 14.0%, p = NS) as well as current smokers and former smokers (4.4% *vs*. 9.9%, p = NS). Although after exclusion of subjects presenting with cardiogenic shock absolute mortality rates substantially decreased, trends towards lower in-hospital mortality in smokers persisted (Fig. 2). However, mortality rates in the setting of primary PTCA in patients without symptoms of cardiogenic shock were comparable when analysed separately in current smokers, former smokers and non-smokers (1.2% *vs*. 4.7% *vs*. 5.2%, p for all comparisons = NS). We noticed a high in-hospital mortality in subjects with STEMI complicated with cardiogenic shock, with no difference relating to smoking status (41.7% *vs*. 56.2%, p = NS).

The total duration of hospitalisation was similar in smoking and non-smoking patients (5.3 ± 5.4 days *vs*. 5.1 ± 5.9 days, p = NS). As far as the relation between the duration of hospitalisation and particular indication for PTCA is concerned, a trend towards prolongation of in-hospital stay was noted in non-smokers suffering from STEMI (SA 3.1 ± ± 5.2 days *vs*. 2.8 ± 3.1 days, p = NS; UA/NSTEMI 6.5 ± 6.6 days *vs*. 7.7 ± 8.9 days, p = NS; STEMI 8.3 ± 4.8 days *vs*. 7.6 ± 4.5 days, p = 0.093).

Multivariate analyses

Smoking status, when adjusted for the baseline characteristics from Tables 1 and 2, did not possess any predictive value in terms of in-hospital mortality (OR for non-smokers *vs*. smokers 1.73, 95% CI 0.61–4.91, p = NS) (Table 3).

Moreover, all considered surrogates of intervention complexity (overall PTCA duration, duration of exposure to X-rays and volume of administered contrast medium) were not influenced by smoking when corrected for variables from Tables 1 and 2.

Discussion

Despite widespread awareness of its deleterious effect, smoking remains the single largest preventable cause of cardiovascular morbidity and premature death in developed countries [19]. Smokers in our study experienced their first STEMI more than a decade earlier when compared to non-smokers. In the INTERHEART trial investigating 27,089 participants from 52 countries current smoking was associated with an almost 3-fold greater risk of non-fatal acute myocardial infarction compared with never smoking. Although the odds ratio for former smokers fell below 2 within 3 years of quitting,

Table 3. Independent predictors of in-hospital mortality in the entire investigated population.

Variable	Variant	OR	95% CI	p
Cardiogenic shock	Present *vs*. absent	35.74	11.39–112.20	< 0.0001
Final flow in the culprit vessel	TIMI 0 or 1 *vs*. TIMI 2 or 3	6.09	1.77–20.99	< 0.005
	STEMI *vs*. SA	10.43	1.72–63.43	< 0.02
	STEMI *vs*. UA/NSTEMI *vs*. SA	3.23	1.31–7.96	
History of diabetes mellitus	True *vs*. false	5.00	1.70–14.73	< 0.004
Gender	Male *vs*. female	3.68	1.13–12.01	< 0.04
History of myocardial infarction	True *vs*. false	2.97	1.06–8.36	< 0.04
Body mass index (BMI)	1 kg/m^2 increase in BMI	1.14	1.01–1.29	< 0.04
Age	1 year increase in age	1.05	1.01–1.10	< 0.03
History of statin therapy	True *vs*. false	0.18	0.06–0.55	< 0.003

SA — stable angina; UA — unstable angina; STEMI — ST-segment elevation myocardial infarction; NSTEMI — non-ST-segment elevation myocardial infarction; OR — odds ratio; CI — confidence intervals

a residual excess risk persisted 20 or more years after quitting [20].

Paradoxically, thrombolytic trials consistently revealed lower mortality rates among smokers suffering from STEMI, ranging from 2.3–4.7% in current smokers to 5.2–7.6% in former smokers and 7.0–13.8% in non-smokers [21]. These reports receive inappropriate attention in the lay press and are often cited by smokers as another excuse for not giving up their habit [22]. Various mechanisms underlying the phenomenon were proposed. Postmortem and angiographic studies postulated thrombosis as the predominant cause of acute coronary syndromes in smokers while critical residual coronary stenoses were more frequently found in non-smokers [12, 14]. Pathologic observations from victims of sudden coronary death indicated that smoking cigarettes increased the risk of plaque rupture and acute thrombosis of a lipid-rich, thin-capped atheroma in men [23]. In contrast, in female smokers plaque erosion with superimposed thrombosis was the prevailing mechanism [24]. Furthermore, hypercoagulable states including hyperfibrinogenemia, increased platelet aggregation, and more platelet-dependent thrombin generation was attributed to the greater thrombus burden as well as its particular susceptibility to thrombolysis in smokers [25]. In support of this hypothesis, thrombolytic trials reported higher rates of TIMI grade 3 flow restoration in the infarct-related artery in smokers than in non-smokers [12, 13, 26, 27]. According to latest studies, smoking stimulates the development of collateral circulation [28, 29]. Albeit, due to limited sample sizes we can not exclude the confounding effect of diabetes mellitus, more frequent in non-smokers, that impairs recruitment of collateral vessels [30, 31]. Another explanation for the smoker's paradox in the thrombolytic era may be fewer coexisting high-risk features (older age, diabetes, chronic heart failure, hypertension) in smokers with STEMI [12, 13, 32, 33]. However, after publication of an extensive analysis of over 500,000 STEMI patients undergoing thrombolysis the theory suggesting that baseline characteristics entirely account for unfavourable in-hospital prognosis is not commonly believed [34]. A large international registry revealed a higher in-hospital utilization of evidence-based therapies such aspirin, thrombolytics, glycoprotein IIb/IIIa receptor inhibitors, beta-blockers and statins in smokers when compared to non-smokers across a broad spectrum of acute coronary syndromes [35].

We observed a strong trend towards lower unadjusted in-hospital mortality rates among smokers with STEMI and UA/NSTEMI treated interventionally when compared to non-smokers. However, non-smokers were characterized by their older age than smokers as well as numerous comorbidities that adversely affected prognosis. Therefore, after correction for the baseline characteristics smoking was no longer associated with more favourable in-hospital outcomes. The higher proportion of smokers than non-smokers diagnosed with acute coronary syndromes in our study should be interpreted with caution. Smokers may be more prone to develop vulnerable plaques and hence have more episodes of acute myocardial ischemia. On the other hand, they may be less likely to be referred for elective procedures.

Our data represent a wide spectrum of consecutive patients referred to the catheterisation laboratory for coronary angioplasty. In the real world setting, we confirm observations concerning the smoker's paradox derived mostly from post hoc analyses of randomised trials recruiting highly selected subjects [36–38]. Many of these studies excluded subjects presenting with cardiogenic shock [36, 37] who constitute a particularly challenging subgroup accounting for a substantial proportion of mortality. Similarly, elderly patients as well as subjects with serious or disabling conditions such as chronic heart failure and previous stroke have only a slender representation in these trials. Our material extends observations formulated on the basis of very few studies recruiting unselected patients to contemporary clinical practice with frequent utilization of evidence-based medical therapies and interventional devices.

Weisz et al. [37] analysing data obtained in the randomised CADILLAC trial found the lowest mortality in current smokers, intermediate in former smokers, and highest in non-smokers at 30 days (1.3% *vs*. 1.7% *vs*. 3.5%, respectively, p = 0.02) and 1 year (2.9% *vs*. 3.7% *vs*. 6.6%, respectively, p = = 0.0008). In addition, rates of reinfarction were lower in current smokers during 1-year follow-up period, resulting in lower composite rates of major adverse cardiac events in cigarette smokers. Indeed, a "dose-response" curve was evident, with the greatest protection from mortality and reinfarction in those who smoked the most. However, after a multivariate correction for differences in baseline variables, current smoking status was no longer protective against late mortality in this low-risk population with STEMI.

In a subanalysis of PAMI trial non-smokers (n = 128) treated with primary PTCA for STEMI had a lower frequency of in-hospital death and

nonfatal recurrent myocardial infarction (7% *vs*. 18%, p = 0.05), in-hospital ischemia (11% *vs*. 33%, p = = 0.004), or the combined event (13% *vs*. 40%, p = = 0.001) compared with counterparts who were given tissue plasminogen activator [36]. Conversely, in smokers (n = 168), the treatment strategy did not significantly affect hospital outcomes: recurrent ischemia (12% *vs*. 23%, p = 0.07), death and recurrent AMI (6% *vs*. 8%, p = 0.55), or the combined event (15% *vs*. 25%, p = 0.12). Quite the opposite to PAMI investigators, Hasdai et al. [38] found from analysis of the GUSTO IIb study that primary PTCA was associated with a better 30-day outcome than tissue plasminogen activator, regardless of smoking status.

Contrary to the CADILLAC trial, Kinjo and coworkers after an analysis of 2,579 patients with acute myocardial infarction from the OACIS study found a markedly higher adjusted mortality in persistent smokers than in non-smokers (hazard ratio 2.27; 95% CI 1.17–4.44) during an average follow-up of 885 days [39]. Additionally, smoking cessation was identified as an independent predictor of reduced mortality (hazard ratio 0.39; 95% CI 0.20–0.77). Study participants were predominantly (> 80%) treated with primary PTCA.

Gąsior et al. [40] evaluating a large cohort of consecutive patients (n = 1,176) from the Silesian Centre for Heart Disease treated mainly with provisional stenting for STEMI concluded that differences in the baseline characteristics (younger age of smokers and less female, diabetic or hypertensive subjects in the smoking group) have a crucial impact on better in-hospital outcome in smokers. What is more, investigators noted a higher incidence of cardiogenic shock among non-smokers (16% *vs*. 8%, p < 0.001). After an adjustment for the clinical characteristics, smokers and non-smokers did not differ in terms of in-hospital mortality. However, in our material, in comparison to the data from Zabrze, stents were implanted much more frequently (82.2% *vs*. 59.2%) and a remarkably high proportion of patients received abciximab (18.6% *vs*. 4.7%), which reflects contemporary standards in interventional cardiology. Direct comparison between studies may also be affected by a substantial number of rescue PTCA procedures performed after failed thrombolysis (n = 433) in the cited study. Due to full coverage of our region by interventional centres providing primary PTCA in STEMI, such patients are very infrequent in our institution. All cases of interventions in STEMI in our study were primary PTCA.

Due to a greater thrombotic component, smokers presenting with acute coronary syndromes may derive particular benefit from a potent antiplatelet therapy. Subanalysis of REPLACE-2 trial indicated that smokers (n = 1,558) undergoing percutaneous coronary interventions on adjunctive treatment with bivalirudin had an absolute 3.2% increase in the composite end point of death and myocardial infarction at 48 hours compared with smokers who were treated with heparin and abciximab (7.7% *vs*. 4.5%, p = 0.008) [41]. This effect was absent in 4,305 non-smokers as well as in the general population. Based on such suggestions and considering age-related risk of bleeding, operators from our centre were more likely to administer abciximab to smokers.

Conflicting data regarding the role of smoking on the outcomes of the elective PTCA procedures have been published. Hasdai et al. [42] reported that current smokers undergoing elective PTCA had fewer adverse events than non-smokers and former smokers and less often required repeat revascularizations during a mean of 4.5 years. What is of great importance is that persistent smokers, after correction for the baseline characteristics, were at higher risk for both death and Q-wave myocardial infarction. Unfortunately, due to limited follow-up, we did not evaluate this problem in our material. Other studies found similar [43] or increased [44] rates of restenosis after elective PTCA in smokers. Finally, Cohen et al. [45] after a retrospective analysis of 8,671 patients from 9 trials concluded that smoking was associated with lower rates of target lesion revascularizations with no impact on angiographic restenosis. Several possible explanations for lower repeat (target and non-target) revascularization rates were proposed [42]. Firstly, physicians may be reluctant to perform subsequent PTCA procedures in patients who continue to smoke. Secondly, a slightly higher proportion of smokers in comparison to non-smokers in whom complete revascularizations was achieved may necessitate further interventions in the latter group. And thirdly, more frequent risk factors for CAD (diabetes mellitus, hypertension) in non-smokers accelerate the progression of coronary atherosclerosis.

Major study limitations include its retrospective character, the use of registry data and single centre experience. Due to the relatively infrequent incidence of end point events the study may be underpowered to differentiate between current and former smokers. Therefore, in numerous analyses we compared ever smokers with non-smokers. In addition, the patients' reporting of their smoking status may not have been accurate in all cases. The study results apply only to patients who reached the

hospital. A considerable numbers of patients with acute coronary syndromes die before admission. The issue of whether or not smoking status influences prehospital mortality rates is still a subject of discussion. In the only study known to us, which addresses this problem, smokers (n = 2,166) when compared to non-smokers (n = 1,088) had a higher risk of dying before hospital admission but the difference was not significant (OR 1.09; 95% CI 0.93–1.27) [46]. However, unexpectedly high prehospital mortality rates (38.4% in smokers *vs*. 37.6% in non-smokers) question the credibility of these findings. We also investigated a heterogeneous population in terms of CAD manifestation. Even though we adjusted for the clinical presentation in a multivariable analysis, deaths occurred mostly in STEMI patients. Additionally, it would be valuable to extend follow-up beyond the hospital discharge.

Conclusions

To conclude, a strong trend towards decreased mortality among smokers undergoing PTCA was observed when compared to non-smokers. The survival advantage is not a consequence of smoking status per se making the commonly used term "smoker's paradox" misleading. This difference may be fully explained by the younger age of smokers, their more favourable clinical characteristics and less extensive coronary atherosclerosis. In fact, smoking contributes to the occurrence of acute coronary syndromes at a younger age and no convincing evidence concerning a protective role of smoking in the interventional setting exists. Finally, bearing in mind the results of primary and secondary prevention trials clearly indicating beneficial effects of a non-smoking lifestyle and smoking cessation, any form of smoking should be strongly discouraged.

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