One-year clinical outcome after emergency hospitalisation for suspected acute coronary syndrome – a comparative analysis with respect to angiographic findings

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Abstract

Introduction: Among patients with suspected acute coronary syndromes (ACS) referred for urgent coronary angiography there are some with normal angiograms.

Aim: To compare, with respect to angiographic findings, one-year clinical outcomes in patients hospitalised for suspected ACS.

Method: Between January 2001 and December 2003 emergency angiography was performed in 1169 patients. It revealed no significant coronary lesions in 97 (8.3%) cases, of these 40 being women and 57 men with a mean age of 55±15 yrs (Group 1). Sixty consecutive patients with ACS (20 women and 40 men with a mean age of 54±9 yrs) and significant coronary artery disease (CAD) confirmed by angiography were the study controls (Group 2). Demographic data, CAD risk factors, angiographic findings, ECG and echocardiographic data as well as laboratory test results were analysed. In a long-term follow-up, the prevalence of recurrent angina and all-cause mortality were assessed.

Results: There were no significant differences in patients' demographics between the two groups with the exception of arterial hypertension, which was more frequent in group 1. In group 1 the diagnosis of ACS was established in 14.5% cases, X syndrome in 14.4%, Prinzmetal angina in 4.1%, myocarditis in 6.1% and pulmonary thromboembolisation in 5.1%. A definite diagnosis was not related to the cardiovascular disease in 36%. No complications were observed in the late follow-up of group 1 patients.

Conclusions: Apparently normal angiograms are relatively common in patients referred for emergency coronary angiography. In patients without significant CAD on their angiograms the clinical outcome is favourable, without major adverse cardiovascular events in the long-term follow-up.

Key words: acute coronary syndrome, normal coronary angiography

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Introduction

In about 20-30% of patients referred for elective coronary angiography due to angina or positive treadmill ECG tests angiograms of epicardial arteries are apparently normal [1]. Among them there is a special subgroup of patients admitted to hospitals with electrocardiographic indices of acute coronary syndrome (ACS) (with or without ST elevation) who are referred for emergency angiography. These patients account for 1-3% of all emergency angiograms [2]. The aim of the study was to compare, with respect to angiographic findings, one-year clinical outcomes in patients hospitalised for suspected ACS.

Methods

Patients

There were 1169 patients admitted to the interventional cardiology unit between January 2001 and December 2003 who underwent angiographic examination (Figure 1). Ninety-seven (8.3%) were either apparently normal or showed insignificant lesion

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angiograms in 40 women and 57 men with a mean age of 58±15 years. The control group consisted of 60 consecutive patients (20 women and 40 men, mean age 55±10 years) with ST elevation ACS and angiographic confirmation of significant coronary artery disease (CAD) (defined as lumen reduction >75% DS) (group 2).

All angiograms of group 1 patients were visually assessed (lesion significance) and with respect to the magnitude of the artery lumen reduction divided into the following three categories:

- coronary arteries without any atherosclerotic changes;
- insignificant lesions (defined as <20% lumen reduction, %SD);
- muscle bridging with systolic blood flow impairment.

Left ventricular (LV) apical contractility was assessed based on left-sided ventriculography in patients hospitalised in 2003.

In order to evaluate the course of the disease and CAD risk factors (arterial hypertension, diabetes, smoking, lipid abnormalities, obesity and family history), a retrospective analysis of hospital records as well as clinical data gathered during the follow-up was conducted in both groups.

The type of ACS, i.e. with or without ST elevation, as well as infarct localisation, were defined based on ECG recordings that were the reason for a patient's referral to our institution.

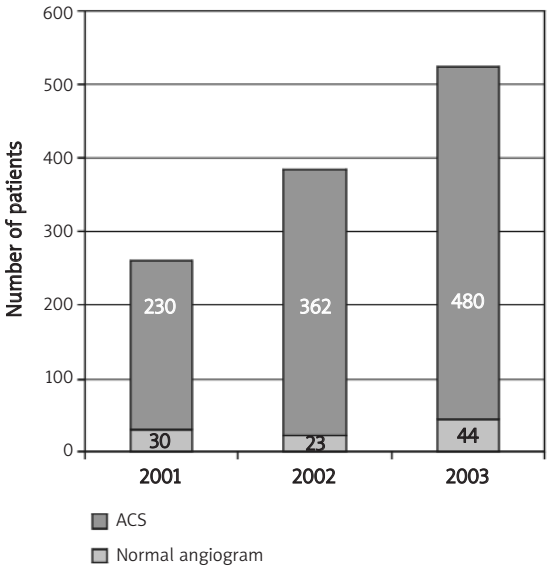

Figure 1. Patients admitted for emergency angiography with respect to a definite diagnosis of acute coronary syndrome or normal coronary arteries

In all patients echocardiography was performed on a regular basis. The ejection fraction (EF-%) was estimated and regional contractility abnormalities as well as other possible causes of clinical symptoms, including pericarditis, valve incompetence and aortic dissection, were sought for.

In hospital, myocardial injury markers were repeatedly measured (phosphocreatine kinase – CK; CK-MB fraction – CK-MB; troponin I levels) in both groups.

Definitions

ST-elevation myocardial infarction (STEMI) was defined by a triad of a typical chest pain, persistent ST-segment elevation, and at least a threefold increase in levels of cardiac biomarkers.

Acute coronary syndrome without ST-segment elevation (NSTE ACS) was diagnosed if the typical chest pain was accompanied by ST-segment depression or T-wave inversion on ECG, irrespective of the cardiac biomarkers surge.

Syndrome X was defined as the presence of typical angina, confirmed by a positive stress test (treadmill test, for instance) and absence of angiographic CAD.

Prinzmetal angina was diagnosed when during angiography a coronary artery spasm could be observed that correlated with angina and ECG changes (mainly ST elevation) corresponding with the offending vessel supply area.

Myocarditis was characterised by elevated myocardial injury biomarkers and indices of inflammation (temperature, CRP and leucocytosis) confirmed by either typical histological findings in myocardial biopsy specimens or positive tests for cardiotropic viruses in peripheral blood samples.

Pulmonary thromboembolism was diagnosed based on clinical signs and symptoms (dyspnoe, tachycardia, tachypnoe, haemoptysis) that were associated with abnormal blood gases, increased levels of D-dimers and presence of thrombus in helical CT or echocardiography.

Transient LV apical ballooning (TLVAB) was defined as the presence of ECG changes, positive cardiac markers and regional wall motion abnormalities (assessed by left ventriculography) such as hypokinesia or akinesia of apical and periapical segments of the anterior and inferior wall with hyperkinetic performance of the remaining segments.

During the follow-up (by means of a questionnaire or outpatient evaluation – after a mean period of 12 months) angina recurrence (including rehospitalisations), need for hospitalisation, repeated coronary angiography and revascularisation as needed (PCI or CABG) and fatal events were assessed.

Results

There were no gender or age differences between the groups. The mean age was 55±15 yrs (41% women) in group 1 and 55±10 yrs (38% women) in group 2.

The prevalence of CAD risk factors was similar in both groups with the exception of arterial hypertension, which was more frequent in group 1 ($p<0.05$, Figure 2).

Forty-six (47%) patients in group 1 were admitted to the hospital with suspected STEMI and 51 (53%) patients with NSTE ACS. All patients in group 2 were hospitalised for suspected STEMI.

In group 1, the definite diagnosis based on a complete clinical work-up, including angiography, was STEMI in only 6 (6.1%) cases and NSTE ACS in 13 (13.4%). Definite diagnoses in the remaining patients are shown in Figures 3 and 4.

In group 1, angiography revealed no CAD in 54 (55%) cases and myocardial bridging of the left descending artery (LAD) in 6 (10.8%) cases (Figures 5 and 6). An insignificant diffuse CAD was found in 34 (45%) patients.

Although in group 1 the mean CK value was 320±404 U/L, CK-MB 38±44 U/L and troponin I 10±21 ng/ml, it is of note that troponin I levels in 43 (44%) patients were within the normal range (0.0-0.2 ng/ml). Levels of these markers were significantly higher in group 2 and reached levels of 2731±80 U/L, 238±111 U/L, and 41±27 ng/ml, respectively ($p<0.05$).

In the follow-up period (mean 12±4 months) there were five (5.6%) deaths in group 1 and ten deaths (16.7%) in group 2 ($p<0.05$). In group 1 there were no fatal cardiovascular (CV) events, four patients died of cancer and one committed suicide. In group 2 there were eight CV (13.3%) deaths and two patients died of cancer.

Angina recurrence was observed in 9 (9.2%) and 23 (38%) patients in groups 1 and 2, respectively. Nineteen patients suffering from recurrent symptoms in group 2 underwent second angiography and none of the patients in group 1 presenting similar symptoms had a repeated examination (mainly due to a negative angiogram at the time of initial presentation). There were 14 (23.3%) patients in group 2 who underwent redo revascularisation procedure.

Late outcomes in 19 patients of group 1 with confirmed ACS were similar to group 2 patients.

Discussion

No reports have been published presenting detailed data on the prevalence of normal angiograms in patients referred for emergency angiography with suspected ACS. In our study population this phenomenon occurred in 8.3% of patients. The number of such patients may not be so small if we remember

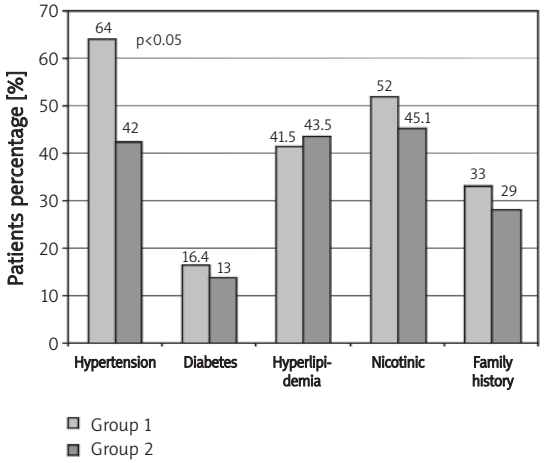

Figure 2. Distribution of coronary artery disease risk factors in groups 1 and 2.

that in Poland about 20 000 patients undergo emergency coronary angiography each year (n=1600).

Although the indications for angiography in STE ACS are well established, it remains somewhat controversial to proceed with the examination in NSTE ACS. NSTE ACS were suspected in over half of group 1 patients and elevated troponin level was considered an indication for angiography. New ESC/ACC criteria for MI diagnosis, introduced in 2000, stress that any myocardial necrosis caused by ischaemia should be referred to as infarction [3]. Excessive cardiac load and toxic injury are examples of non-ischaemic myocardial damage [4]. Pericarditis [5], severe congestive heart failure [6], pulmonary embolisation [7], direct myocardial injury (ablation and cardiosurgical procedures, chest and heart trauma), toxic drug injury (adriamycine, 5-fluorouracyl) [8], viral myocarditis [9],

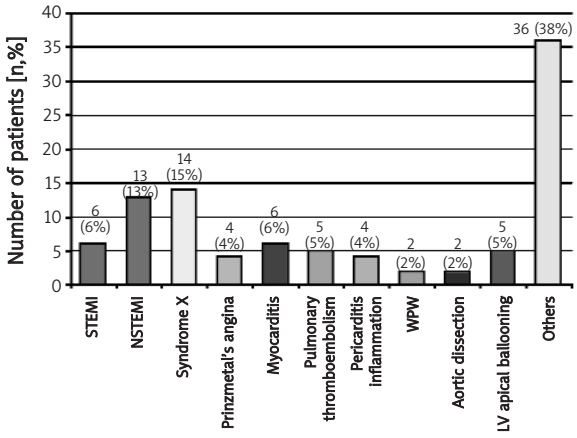

Figure 3. Definite diagnoses in group 1

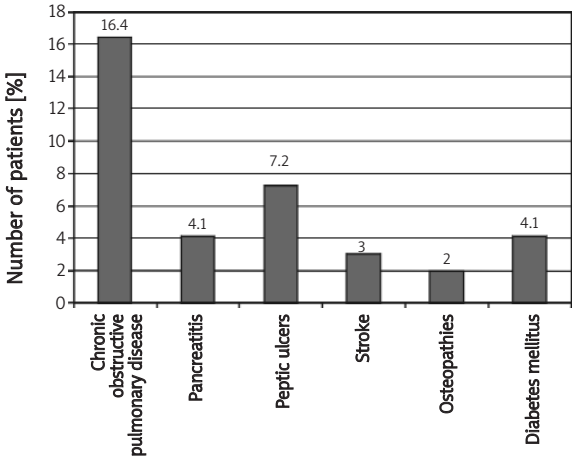

Figure 4. Non-cardiac-related definite diagnoses in group 1

cerebral vascular disease [10], sepsis [11], rheumatoid arthritis [12] and renal dysfunction (TnT) [13] may also be causes of positive troponin tests.

In our study cardiac syndrome X was diagnosed in 14% of patients. In these patients angiograms very often revealed slower epicardial contrast flow, probably due to either functional endothelial dysfunction or vascular wall hypertrophy [14-16]. Abnormal reactivity of coronary arteries seems to be one of the possible mechanisms, with underlying endothelium dysfunction and imbalance between endothelial production and release of vasoactive factors [17, 18]. Patients suffering from syndrome X generally have a favourable prognosis [19].

According to published reports, in about 1% of ACS in patients without epicardial CAD in angiography muscle bridges are responsible for these events. The prevalence of muscle bridges in our series (6%) is much higher. It is thought that muscle bridging may lead to significant ischaemia if it reduces the blood flow rate by at least 75% [20-22].

Coronary artery spasm is another possible cause of acute coronary syndrome. It may involve either slightly stenotic or normal coronary segments. The usual clinical presentation of such spasms are recurrent anginal episodes with concomitant ECG changes, but they may also cause sudden cardiac death [23-25]. Although there were four patients suffering from Prinzmetal angina in our study, no late complications were observed.

Standard left ventriculography has been performed following the normal angiograms since the beginning of 2003. As a result five cases of TLVAB, which mimics NSTE-ACS [26]. In the study population TLVAB was found in over 10% of patients with insignificant CAD and accounted for 1% of all emergency angiographies in ACS. It seems obvious that we must have missed such cases in the past.

According to the results of published studies, one of the most important risk factors of ACS in patients with normal angiograms is cigarette smoking [27]. However, prognosis in such patients is better than in patients with angina and confirmed coronary artery involvement. Not

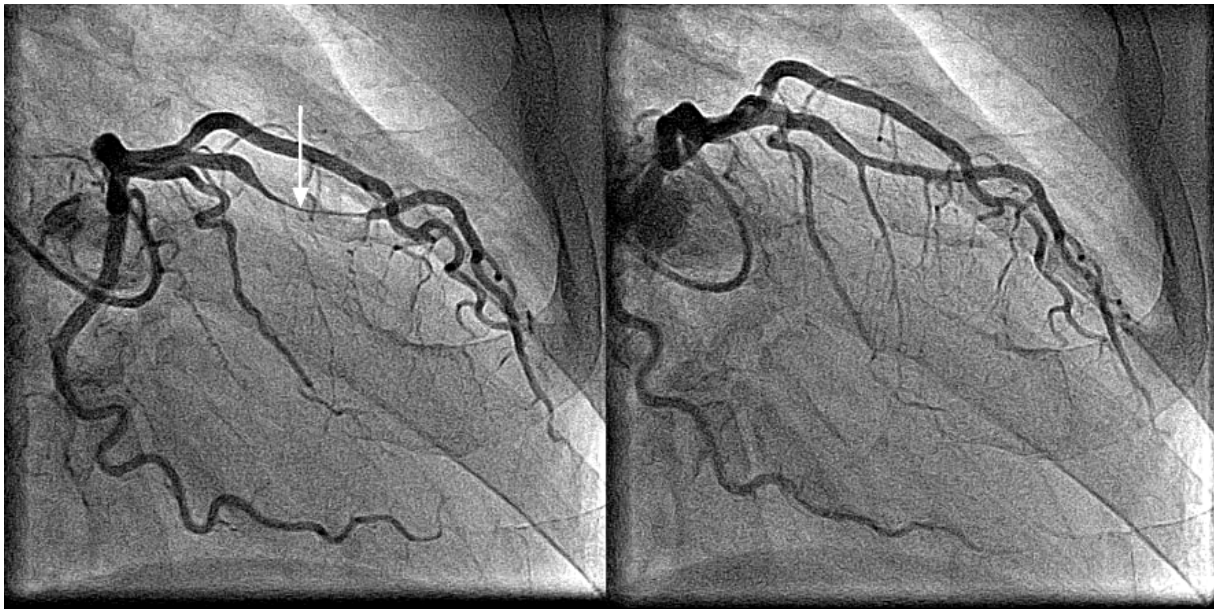

Figure 5. Angiogram of a patient with suspected ACS. Muscular bridging of the left descending artery is present (arrow)

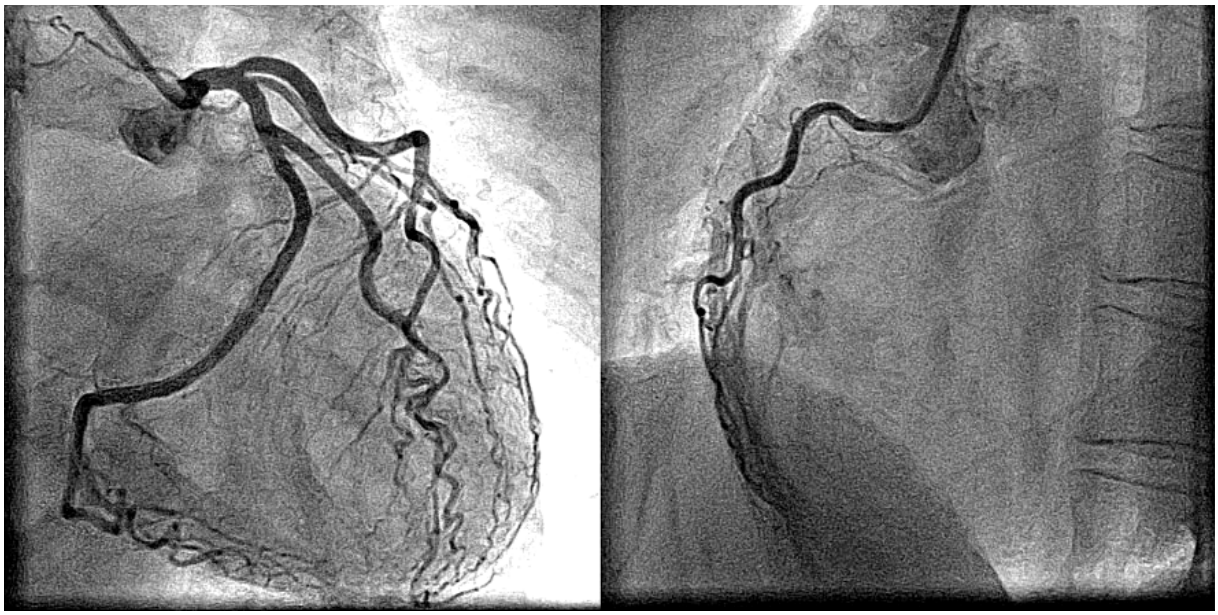

Figure 6. Normal angiogram of a patient admitted for suspected antero-lateral myocardial non-Q-wave infarction

only angina recurrence but also MI, congestive heart failure and sudden cardiac death are less frequent in this population [28]. There was an insignificant trend toward more frequent cigarette smoking in the population without CAD in our study.

Except for more frequent arterial hypertension in patients with normal angiograms, there were no differences in the prevalence of CAD risk factors between the two groups. It is plausible that myocardial hypertrophy, associated with arterial hypertension, could under certain circumstances (e.g. sudden blood pressure rise) cause ischaemia in some group 1 patients with all the consequences.

The high prevalence of non-cardiac diseases in our patients is noteworthy. Similar or indistinguishable symptoms, various ECG changes and non-specific increases in biomarkers frequently lead to a false initial diagnosis. One possible explanation is the increased availability of emergency angiography. Having in mind the experienced interventional cardiologists available, the better knowledge of ACS and the relatively low risk of coronary angiography, physicians currently are more eager to qualify patients with comorbidities or the elderly for emergency examinations.

There are reports suggesting that the late outcome in patients aged >75 years is improved to a similar extent, regardless of whether diagnostic angiography or PCI is performed [29]. With anatomical knowledge of the coronary tree, the subsequent surgical revascularisation may be precisely planned.

As in ACS time is a critical factor, we tend to shorten our diagnostic pathway. We believe that prompt exclusion of suspected ACS is more reasonable than prolonging the decision-making time.

Study limitations

Owing to the small number of patients with a definite diagnosis of ACS and normal coronary angiograms (n=19), the late outcome comparison with group 2 patients has limited value. Additionally, because in as many as 37% of group 1 patients no cardiovascular disease was found, it must have resulted in a lower rate of CV complication rate in the long-term follow up as compared with group 2 patients.

Conclusions

1. Apparently normal angiograms are relatively common in patients referred for emergency coronary angiography.
2. In patients without significant CAD on their angiograms the clinical outcome is favourable without major adverse cardiovascular events in the long-term follow-up.

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Analiza porównawcza rocznego przebiegu klinicznego chorych hospitalizowanych ze wstępnym rozpoznaniem ostrego zespołu wieńcowego w zależności od angiograficznego obrazu tętnic nasierdziowych

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Streszczenie

Wstęp: Wśród populacji pacjentów kierowanych na pilną koronarografię z powodu podejrzenia ostrego zespołu wieńcowego (OZW) znajdują się też pacjenci z obrazem prawidłowych naczyń wieńcowych.

Cel: Analiza porównawcza rocznego przebiegu klinicznego pacjentów hospitalizowanych ze wstępnym rozpoznaniem OZW w zależności od stwierdzanych w koronarografii zmian miażdżycowych.

Metody: W okresie styczeń 2001-grudzień 2003 r. pilne badania koronarograficzne wykonano u 1169 chorych, przy czym u 97 (8,3 %) osób (40 K+57 M, śr. wieku 55±15 lat) nie stwierdzono zmian w tętnicach wieńcowych (grupa 1). Grupę kontrolną (Grupa 2) stanowiło 60 kolejnych chorych (20 K+40 M, śr. wieku 54±9 lat) z OZW, u których stwierdzono istotne zmiany miażdżycowe. U wszystkich chorych analizowano dane demograficzne, czynniki ryzyka, angiografię tętnic wieńcowych oraz dane uzyskane z badań EKG, echokardiografii i badań labolatoryjnych. W okresie obserwacji odległej analizie poddano nawrót dolegliwości stenokardialnych, a także wystąpienie zgonu.

Wyniki: Nie stwierdzono różnic pomiędzy analizowanymi grupami z wyjątkiem częstszego występowania nadciśnienia tętniczego w grupie 1. W grupie 1 u 19,5% chorych rozpoznano OZW, u 14,4% chorych rozpoznano zespół X, u 4,1% dusznicę bolesną typu Prinzmetala, u kolejnych 6,1% zapalenie mięśnia sercowego, u 5,1% rozpoznano zatorowość płucną. U 36% postawiono rozpoznania nie związane z patologią układu sercowo-naczyniowego. W okresie obserwacji odległej nie stwierdzono istotnych powikłań w grupie 1.

Wnioski: Występowanie obrazu prawidłowych angiograficznie tętnic wieńcowych jest stosunkowo częste w populacji chorych kierowanych do pilnej koronarografii. Rokowanie pacjentów z prawidłowymi angiograficznie tętnicami wieńcowymi jest dobre i nie wiąże się z istotnymi epizodami sercowo-naczyniowymi w okresie obserwacji odległej.

Słowa kluczowe: ostry zespół wieńcowy, prawidłowa koronarografia

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