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Significant decrease in in-hospital mortality and major adverse cardiac events in Swiss STEMI patients between 2000 and December 2007

THESE

préparée sous la direction du Professeur honoraire Lukas Kappenberger jusqu'en mai 2008, puis du Docteur Jean-Christophe Stauffer, Privat-Doctent et Maître d'Enseignement et de recherche avec la co-direction du Professeur titulaire Pierre Vogt

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par

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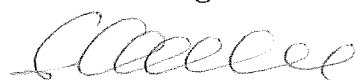
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*Significant decrease in in-hospital mortality and major
adverse cardiac events in Swiss STEMI patients between 2000
and December 2007*

Lausanne, le 27 octobre 2009

pour Le Doyen
de la Faculté de Biologie et de Médecine



Madame le Professeur *Stephanie Clarke*
Directrice de l'Ecole doctorale

Rapport de synthèse

Objectifs : évaluer la survie intra-hospitalière des patients présentant un infarctus du myocarde avec sus-décalage du segment ST admis dans les hôpitaux suisses entre 2000 et 2007, et identifier les paramètres prédictifs de mortalité intra-hospitalière et d'événements cardio-vasculaires majeurs (infarctus, reinfarctus, attaque cérébrale).

Méthode : utilisation des données du registre national suisse AMIS Plus (Acute Myocardial Infarction and Unstable Angina in Switzerland). Tous les patients admis pour un infarctus du myocarde avec sus-décalage du segment ST ou bloc de branche gauche nouveau dans un hôpital suisse participant au registre entre janvier 2000 et décembre 2007 ont été inclus.

Résultats : nous avons étudié 12 026 patients présentant un infarctus du myocarde avec sus-décalage du segment ST ou bloc de branche gauche nouveau admis dans 64 hôpitaux suisses différents. L'âge moyen est de 64 ± 13 ans et 73% des patients inclus sont des hommes. L'incidence de mortalité intra-hospitalière est de 7.6% en 2000 et de 6% en 2007. Le taux de réinfarctus diminue de 3.7% en 2000 à 0.9% en 2007. L'utilisation de médicaments thrombolytiques chute de 40.2% à 2% entre 2000 et 2007. Les paramètres prédictifs cliniques de mortalité sont : un âge > 65 ans, une classe Killips III ou IV, un diabète et un infarctus du myocarde avec onde Q (au moment de la présentation). Les patients traités par revascularisation coronarienne percutanée ont un taux inférieur de mortalité et de réinfarctus (3.9% versus 11.2% et 1.1% versus 3.1%, respectivement, $p < 0.001$) sur la période de temps étudiée. Le nombre de patients traités par revascularisation coronarienne percutanée augmente de 43% en 2000 à 85% en 2007. Les patients admis dans les hôpitaux bénéficiant d'une salle de cathétérisme cardiaque ont un taux de mortalité plus bas que les patients hospitalisés dans les centres sans salle de cathétérisme cardiaque. Mais les caractéristiques démographiques de ces deux populations sont très différentes.

La mortalité intra-hospitalière ainsi que le taux de réinfarctus diminuent significativement au cours de la période étudiée, parallèlement à l'augmentation de l'utilisation de la revascularisation coronarienne percutanée. La revascularisation coronarienne percutanée est le paramètre prédictif de survie le plus important.

Conclusion : la mortalité intra-hospitalière et le taux de réinfarctus du myocarde ont diminué de manière significative chez les patients souffrant d'un infarctus du myocarde avec sus-décalage du segment ST au cours de ces sept dernières années, parallèlement à l'augmentation significative de la revascularisation coronarienne percutanée en plus de la thérapie médicamenteuse. La survie n'est pas liée au lieu d'hospitalisation mais à l'accès à une revascularisation coronarienne percutanée.

Significant decrease in in-hospital mortality and major adverse cardiac events in Swiss STEMI patients between 2000 and December 2007

Results from the AMIS registry

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^f Acute myocardial infarction and unstable angina in Switzerland (AMIS Plus)

Summary

Objectives: To evaluate the in-hospital outcome of STEMI (ST elevation myocardial infarction) patients admitted to Swiss hospitals between 2000 and December 2007, and to identify the predictors of in-hospital mortality and major cardiac events.

Methods: Data from the Swiss national registry AMIS Plus (Acute Myocardial Infarction and Unstable Angina in Switzerland) were used. All patients admitted between January 2000 and December 2007 with STEMI or a new LBBB (left bundle branch block) were included in the registry.

Result: We studied 12 026 STEMI patients admitted to 68 hospitals. The mean age was 64 ± 13 years and 73% of the patients were male. Incidence of in-hospital death was 7.6% in 2000 and 6% in 2007. Reinfarction fell from 3.7% in 2000 to 0.9% in 2007. Thrombolysis decreased from 40.2% in 2000 to 2% in 2007. Clinical predictors of mortality were: age >65 years, Killips class III or IV, diabetes, Q wave myocardial infarction (at presentation). Patients undergoing percutaneous

coronary intervention (PCI) had lower mortality and reinfarction rates (3.9% versus 11.2% and 1.1% versus 3.1% respectively, $p < 0.001$) over time, although their numbers increased from 43% in 2000 to 85% in 2007. Patients admitted to hospitals with PCI facilities had lower mortality than patients hospitalised in hospitals without it, but the demographic characteristics differ widely between the two groups.

Both in-hospital mortality and reinfarction decreased significantly over the time, parallel to an increased number of PCI. PCI was also the strongest predictor of survival.

Conclusion: In-hospital mortality and reinfarction rate have decreased significantly in Swiss STEMI patients in the last seven years, parallel to a significant increase in the number of percutaneous coronary interventions in addition to medical therapy. Outcome is not related to the site of admission but to PCI access.

Key words: myocardial infarction; angioplasty, STEMI, PCI

Introduction

Reperfusion and prompt restoration of antegrade coronary blood flow results in myocardial salvage and improved left ventricular function and survival [1-3] of patients with acute myocardial infarction. Both thrombolytic therapy and percutaneous

coronary intervention (PCI) are used to open the infarct-related artery [4-6]. Several randomised trials favour PCI over thrombolysis [7-16], especially in high risk patients [11, 17] due to a higher patency rate, less reocclusion, recurrent

ischaemia, reinfarction, and stroke [18–21]. Thrombolysis and medical management remain the first choice treatment in some hospitals without PCI capabilities, because of strategic constraints. Previous studies have shown that on site PCI is a major determinant of patient management. However, it is still an open question whether the outcome of patients admitted to hospitals with or without PCI capability is the same

or not, merely because the strategy and the infrastructure are different.

We evaluated the Swiss STEMI (ST elevation myocardial infarction) patients over time to detect change in management (in line with the evolving guidelines) and possibly in their prognosis. We also evaluated the clinical predictors of in-hospital mortality, reinfarction and stroke.

Methods

Data from the Swiss national registry on myocardial infarction AMIS Plus were used.

The AMIS Plus Registry

Since 1997 this Swiss prospective national registry has collected data from patients admitted with a definitive diagnosis of acute coronary syndrome in Switzerland (AMIS Plus). It is a prospective data bank monitored by a Data Centre (Institute of Social and Preventive Medicine at the University of Zürich) providing blinded data of Swiss STEMI and non-STEMI patients. It is a complete cohort of Swiss patients. Data are collected by an internet- and/or paper-based questionnaire of 140 questions, related to patient history, clinical parameters, previous medical history, laboratory parameters, in-hospital and discharge treatment, hospitalisation outcome and destination at discharge. The questionnaire is completed by physicians and research nurses and has been described previously [22].

Patients are enrolled in the registry on the basis of final diagnosis, which must comply with one of the following three definitions: acute myocardial infarction (symptoms or ECG changes compatible with acute coronary syndrome, or both, and cardiac enzymes (total creatine kinase (CK) or CK-MB) at least twice the upper limit of normal range); acute coronary syndrome with minimum necrosis (symptoms or ECG changes compatible with acute coronary syndrome, or both, and cardiac enzymes (total CK or CK-MB) lower than twice the upper limit of normal range, and positive troponins); and unstable angina (symptoms or ECG changes compatible with acute coronary syndrome, or both, and normal cardiac enzymes). Cases that are of unclear or non-cardiac cause are not included.

For this article we analyzed only patients with STEMI.

The project is led by a Steering Committee and was approved by the Supraregional Ethical Committee for Clinical Studies and the Swiss Board for Data Security.

Study population

Between January 2000 and December 2007, patients with STEMI or new left bundle branch block (LBBB) were included in the registry. These patients were filtered out of the AMIS Plus collective according to the discharge diagnosis. American Heart Association/American College of Cardiology (AHA/ACC) guidelines were followed for patient management. Physicians were allowed to use thrombolysis and/or PCI in both types of hospital when needed. Patients hospitalised in establishments without PCI facilities had to be transferred for PCI.

Patient characteristics

Demographic data, clinical variables, procedures, and events were collected at admission and during the hospital stay by physicians and dedicated nurses.

Statistics

All analyses were performed by the AMIS Plus Data Centre. All categorical measures are reported as counts with percentage and valid values. Pearson's chi-square were used for group comparisons. The chi-square tests were two-sided. All p values were two-sided and were considered significant if <0.05 . A multivariate logistic model was used to determine in-hospital mortality predictors from the following set of variables: admission year; age; sex; systolic and diastolic blood pressures; heart rate; history of arterial hypertension; history of dyslipidaemia; history of diabetes; current smoking status; cardiopulmonary resuscitation before admission; defibrillation/cardiopulmonary resuscitation before admission; Killip class at hospital admission (class I as reference category); delay between symptom onset and admission to hospital >6 hours; Q waves on initial ECG; left bundle branch block on initial ECG; ST segment elevation on initial ECG; thrombolysis; primary PCI, cath-lab at hospital of admission. Separate univariate logistical models were first fitted for each variable and then backwards elimination with a significance level of 0.05 was performed. We represent in tables 3 and 4 only the significant predictors of death and major adverse cardiac events (MACE). Missing data are given in the tables and are not included in the analysis.

Results

Baseline characteristics

Patient demographics and characteristics are presented in table 1. A total of 12 026 patients (73% male) with a mean age of 64 ± 13 years were treated for STEMI and included in the database. In-hospital mortality was 6.9%, reinfarction 1.9%

and stroke 1% (table 2). The incidence of death, reinfarction and stroke declined significantly over time from 7.6% in 2000 to 6.5% ($p = 0.004$) in 2007 for mortality, and from 3.7% to 1% ($p < 0.001$) for reinfarction. The incidence of stroke decreased over time from 1.8% in 2000 to

Table 1
Baseline characteristics.

| | |
|------------------------|---------------|
| N | 12 026 |
| Males | 8828 (73%) |
| Mean age | 64 ± 13 years |
| Killip I-II | 11 130 (93%) |
| Killip III-IV | 845 (7%) |
| Q waves (at admission) | 1971 (16.8%) |
| Hypertension | 6200 (54.7%) |
| History of CAD | 5155 (30.2%) |
| Diabetes | 2128 (18.5%) |
| Current smoker | 4711 (41.7%) |
| Dyslipidaemia | 5873 (54.9%) |

CAD: coronary heart disease

Table 2
Patients outcome.

| | All hospitals | Hospitals without 24 h PCI on site | Hospitals with 24 h PCI on site | P value |
|-----------------------|---------------|------------------------------------|---------------------------------|---------|
| In-hospital mortality | 6.9% | 8.3% | 5.8% | <0.001 |
| Reinfarction | 1.9% | 2.8% | 1.3% | <0.001 |
| Stroke | 1.1% | 0.9% | 1.2% | 0.104 |

0.8% in 2007 (p = 0.04). The percentage of patients treated by PCI increased from 43% to attain the high percentage of 85% in 2007.

Patient management is shown in figure 1. Medical treatment without reperfusion was used

in 20%, thrombolysis alone in 7%, primary PCI in 65% and PCI in addition to thrombolysis (facilitated PCI) in 8%. Patients admitted to hospitals without PCI facilities were more prone to receive thrombolysis (23% versus 9%) than those admitted to hospitals with PCI facilities. PCI was more often used in hospitals with PCI facilities in 2000 (67% versus 27%) but this difference was reduced in 2007 (94% versus 71%). Mortality and reinfarction rate were higher in hospitals without catheterisation facilities (table 2), although the population was not fully comparable (mean age 65 ± 11 years versus 63 ± 13 years (p <0.001).

The use of thrombolysis fell from 40.2% in 2000 to 2% in 2007.

Multivariable analysis for in-hospital death and MACE are presented in tables 3 and 4. Age >65, diabetes, Killip class III-IV, Q wave MI (at presentation) and no PCI were the most significant predictors of death and MACE.

Site of hospitalisation (in-house PCI facilities or not) is not a predictor of death (OR 1.1, 95% CI 0.9–1.3) or MACE (OR 0.9, 95% CI 0.8–1.1). Other variables entered (see the statistics section) were not significant predictors.

The difference in mortality and reinfarction is not related to the hospital type but to access to PCI. Reperfusion (PCI and thrombolysis) have a significant positive impact on survival.

Discussion

The AMIS Plus registry is a unique ongoing multicentre project assessing management of acute coronary syndromes in Switzerland. In-hospital mortality and incidence of reinfarction de-

crease significantly as the number of PCI rises. This confirms the benefit of aggressive management of STEMI patients. In-hospital mortality was 6.9%, which is comparable with other European registries (7% mortality in the Euro Heart survey and GRACE [26, 27], 10.4% by MINAP [28], 14% for the Danish registry [29]). Classical clinical predictors of mortality were as in previous trials [30]. As expected, reperfusion (thrombolysis and PCI) was associated with a better outcome. We confirm the impact of PCI facilities on reperfusion strategies. Availability of a catheterisation laboratory will of course favour the use of primary PCI, with some benefit to the outcome. Our findings are in agreement with other observational

Figure 1
Management of patients.

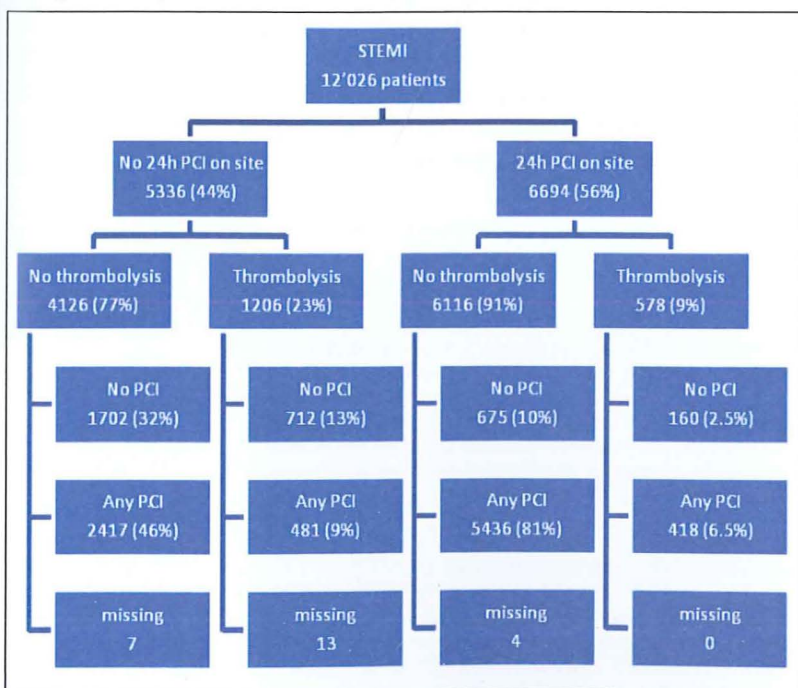


Figure 2
Evolution of PCI, mortality and reinfarction from 2000 to 2007.

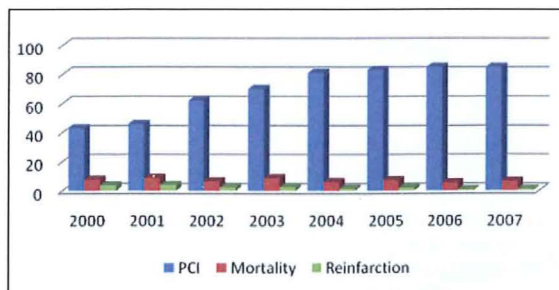


Table 3
Multivariate analysis of predictors of death.

| | OR | 95% CI | P value |
|---------------|-----|----------|---------|
| PCI | 0.5 | 0.4–0.6 | <0.001 |
| Thrombolysis | 0.7 | 0.5–0.9 | 0.008 |
| Killip III–IV | 8.3 | 6.7–10.3 | <0.001 |
| Age >65 years | 3.6 | 2.8–4.5 | <0.001 |
| Diabetes | 1.5 | 1.2–1.8 | <0.001 |
| LBBB | 1.3 | 1.0–1.7 | 0.043 |
| Q waves | 1.3 | 1.0–1.6 | 0.030 |
| >6 h delay | 0.8 | 0.6–1.0 | 0.022 |

Table 4
Multivariate analysis of the composite end point predictors of major adverse cardiac events (death, reinfarction, stroke).

| | OR | 95% CI | P value |
|---------------|-----|---------|---------|
| PCI | 0.6 | 0.5–0.7 | <0.001 |
| Thrombolysis | 0.8 | 0.6–1.0 | 0.057 |
| Age >65 years | 2.8 | 2.3–3.3 | <0.001 |
| Killip III–IV | 6.9 | 5.7–8.5 | <0.001 |
| Q waves | 1.5 | 1.2–1.8 | <0.001 |
| Diabetes | 1.5 | 1.2–1.8 | <0.001 |
| LBBB | 1.2 | 1.0–1.6 | 0.083 |
| >6 h delay | 0.9 | 0.7–1.0 | 0.128 |

registries [13, 21, 23–25]. In the GRACE registry [25] the incidence of in-hospital death was the same between patients treated in hospitals with or without catheterisation facilities, but this registry tested hospital type and not strategy. A different conclusion arises from the recent Swedish registry [31] on long-term outcome of patients with STEMI. A significant reduction in short- and long-term mortality and reinfarction was found when PCI was compared with thrombolysis. We show that on-site PCI is not correlated with a better outcome, but that PCI itself has a favourable impact on mortality and reinfarction. Clearly, access to invasive facilities changes the prognosis of Swiss patients with STEMI. Efforts have been made to improve the proportion of patients transferred from small to larger hospitals with PCI facilities for invasive treatment, and over time the number of these patients increased. This correlated with a reduction in mortality and reinfarction. In addition, we noted that 32% of patients hospitalised in establishments without PCI did not benefit from any type of revascularisation,

compared to 10% of patients hospitalised in establishments with PCI. Even if this is consistent with other recent registries [21, 23, 25], improvements can be made in the application of guidelines and creation of networks to standardise the management of patients with STEMI throughout Switzerland.

Since the AMIS registry is not focused on "lytic eligible patients", it provides real life information and we would not expect 100% access to reperfusion strategies. This is also reported by other groups, e.g., in the DANAMI-2 trial, where only 37% of the cohorts screened were finally included [32]. The differences in terms of reperfusion strategy between two types of hospital changed over time, more patients being transferred for PCI from small hospitals with a significant decrease in mortality.

We conclude that Swiss STEMI patients still have a significant incidence of complications and that management could still be improved by decreasing the time to reperfusion and especially PCI (facilitated communication and teamwork between hospitals). Education of the public is also needed to shorten the time between chest pain and reperfusion.

Study limitations

In essence the AMIS Plus is an observational registry; patients were not randomised to institutions with or without cardiac catheterisation facilities. It is recorded on a voluntary basis and may have been a cause of undetected bias.

Our analysis suffers the limitations of multivariable evaluation, designed to correct raw results according to differences in baseline characteristics.

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