Original article

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Early abciximab use in ST-elevation myocardial infarction treated with primary percutaneous coronary intervention improves long-term outcome. Data from EUROTRANSFER Registry

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Abstract

Background: Primary percutaneous coronary intervention (PCI) is the preferred method of reperfusion in patients with ST elevation myocardial infarction (STEMI). Abciximab is a well established adjunct to primary PCI. The proper timing of abciximab administration in STEMI patients has been investigated in randomised trials, registries and metanalysis, providing conflicting results.

Methods: Consecutive data on STEMI patients, transferred for primary PCI in hospital/ambulance STEMI networks between November 2005 and January 2007, from 15 PCI centres in seven European countries was gathered together for a one-year long-term clinical observation (93% rate of completeness).

Results: Data from 1,650 patients was collected in the EUROTRANSFER Registry. Abciximab was administered to 1,086 patients (66%), 727 patients received early (at least 30 minutes prior to first balloon inflation) abciximab (EA), and another 359 patients received late abciximab (LA). One year mortality was 5.8% in the EA group *vs* 10.3% with LA ($p = 0.007$). Adjustment for propensity score methods for EA administration did not change the results, still providing a favourable outcome for the EA group ($p = 0.004$). It was also revealed that only a minority of patients (36%) were treated within the 90-minute recommended time window from first medical contact to PCI (and 60% for the 120-min time delay).

Conclusions: Patients transferred for primary PCI in STEMI hospital networks showed lower rates of death in long-term one-year clinical follow-up when treatment with abciximab was started early.

Key words: myocardial infarction, percutaneous coronary intervention, abciximab, registry

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INTRODUCTION

Primary percutaneous coronary intervention (pPCI) is the preferred method of reperfusion in patients with ST elevation myocardial infarction (STEMI) [1, 2]. Hospital networking helps facilitate treatment algorithms and decrease time delays in patients transferred for pPCI [3, 4]. The new European STEMI guidelines underline that these delays should not exceed 90–120 minutes. However, even in experienced and well-organised hospital networks, time delays are still substantial [1, 5].

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Pharmacological pre-treatment prior to primary angioplasty has been a concept tested in many trials. Although some have not shown its efficacy [6, 7], others have seen an improvement in surrogate parameters and clinical end-points [8, 9]. Similarly, the proper timing of abciximab administration in STEMI patients has been investigated in randomised trials, registries and metanalysis, providing conflicting results [10–12].

The data from the EUROTRANSFER Registry has added additional evidence as to the early use of abciximab, confirming its high efficacy especially in high risk STEMI patients. It is also one of several studies to observe an improved clinical outcome [13, 14]. The aim of this paper is to present one year clinical follow-up data of the EUROTRANSFER registry patients.

METHODS

EUROTRANSFER Registry was an international, prospective, multicentre European patient registry. Data on STEMI patients transferred for mechanical reperfusion was collected between November 2005 and January 2007 in 15 STEMI networks from seven European countries. The study was registered at ClinicalTrials.gov (NCT00378391). The research plan complied with the Declaration of Helsinki and has been approved by the Jagiellonian University Bioethics Committee in Krakow, Poland. Detailed study design and rationale were outlined in previous papers [13].

Studied groups

Patients who received abciximab at any time of their index pPCI procedure for STEMI were retrieved from the registry database. These patients were divided into two groups: those who received abciximab early, or late. The early abciximab administration (EA group) was defined as starting abciximab before or during transfer to the cath lab, at least 30 minutes prior to first balloon inflation, or coronary angiography in the case of patients who did not undergo pPCI. All other patients who received abciximab within 30 minutes of, or during, pPCI formed the late group (LA group).

Study outcomes

The main clinical outcome parameter in this analysis was death (cardiovascular and all-cause) at one year from index pPCI procedure for STEMI. A follow-up after one year was collected either by patient visit or telephone call (rate of completeness: 93%).

Statistical methods

Data was analysed according to the established standards of descriptive statistics. The primary outcome parameter (death at one year) was adjusted by propensity score for the likelihood of receiving abciximab early [15], using the following 18 variables: sex, age, body mass index, past medical history (previous myocardial infarction, chronic renal failure, heart failure, previous PCI, previous coronary artery bypass grafting, past stroke, current smoker, diabetes mellitus, peripheral artery disease), medications (pre-cath lab clopidogrel and thrombolysis), time from chest pain onset to diagnosis, diagnosis to balloon time and the location where the STEMI diagnosis was made (ambulance or referral hospital). LA and EA group matching was performed. Kaplan-Meier survival curves were plotted for early *vs* late abciximab administration using log-rank test to test for differences.

Statistical significance was defined as a p value < 0.05. All statistical analysis was performed using STATISTICA 8 Software (Statsoft Inc., Tulsa, OK, USA)

RESULTS

Data from 1,650 patients was collected in the EUROTRANSFER Registry. Abciximab was administered to 1,086 patients (66%), 727 patients received early abciximab (EA), and another 359 patients received late abciximab (LA). One year mortality was 5.8% in the EA group *vs* 10.3% with LA ($p = 0.007$). Plotted Kaplan-Meier survival curves are shown in Figure 1. Adjustment for propensity score did not change the results, with early abciximab administration still providing a favourable outcome as seen in Figure 2.

The percentage of patients receiving guideline-recommended therapy within the time window of 90 and 120 minutes is shown in Figure 3. Slightly less than two thirds received it within 120 minutes of first medical contact.

DISCUSSION

Abciximab used as an adjunctive therapy during primary pPCI for STEMI is associated with mortality reduction and is a well-established component of the interventional strategy recommended by the guidelines [1, 16]. However, the recent

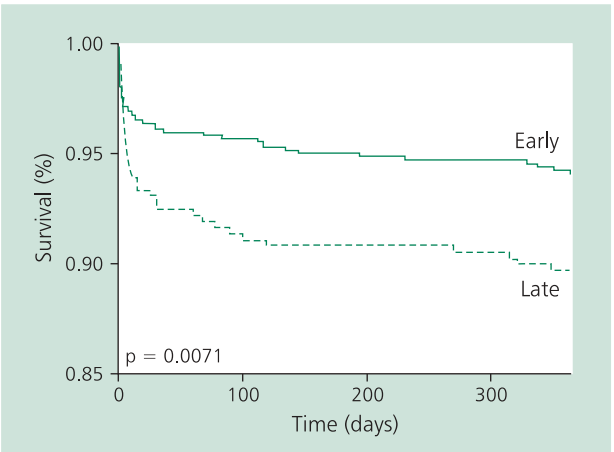

Figure 1. Kaplan-Meier survival curves for early *vs* late abciximab group

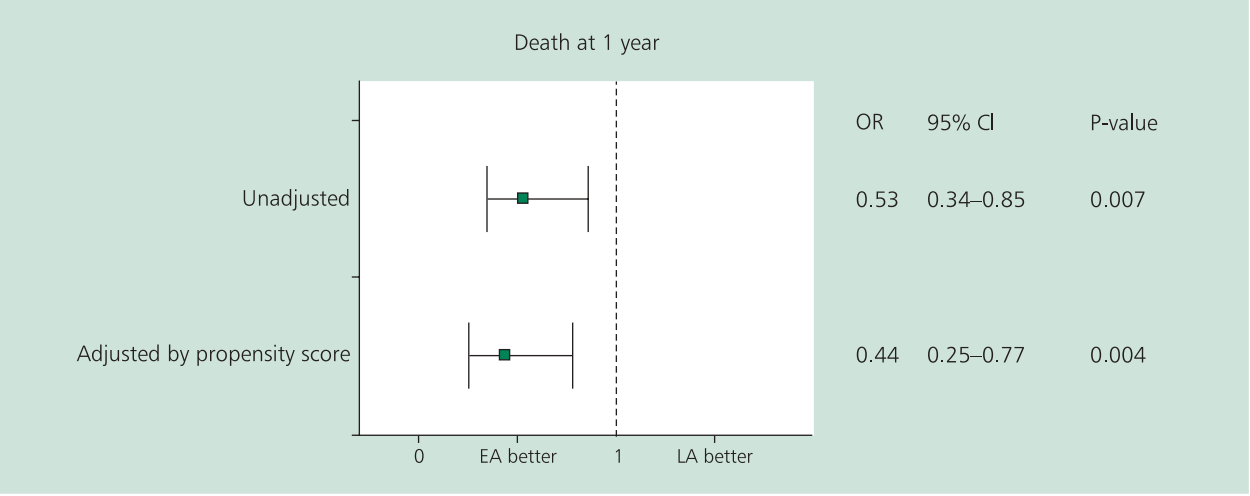

Figure 2. One-year mortality unadjusted and adjusted by propensity score method

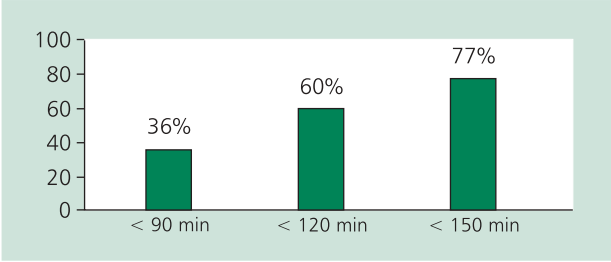

Figure 3. Percentage of patients receiving percutaneous coronary intervention within 90, 120 and 150 minutes of first medical contact in EUROTRANSFER Registry

European STEMI guidelines consider facilitated PCI either with abciximab or lytics as class III recommendation (contraindication) [1]. The US guidelines published by ACC/AHA societies are far more liberal, allowing the use of adjunctive therapies such as abciximab as soon as possible in high risk patients with longer transfer delays and low bleeding risk [17].

Due to conflicting results of studies on abciximab timing in STEMI, it seems vital to track additional results from these trials in order to gather as much data as possible. Subgroup analysis and long-term follow-up can provide valuable information. In the EUROTRANSFER Registry it has already been observed that there is a 30-day immediate mortality reduction in the early abciximab group, even after adjustment by confounders and propensity score methods [13]. The results presented in the current paper confirm these findings at one year follow-up. The benefit of early application of abciximab is constant and once again confirmed after adjustments and is an independent predictor of favourable outcome in multivariate logistic regression analysis [14]. EUROTRANSFER is the first single study to notice such a significant decrease in mortality in long term observation in early *vs* late abciximab use since the ADMIRAL study subanalyses were presented [18]. Moreover, findings from EUROTRANSFER have been recently confirmed by two other trials [19, 20]. Both of these studies report improved surrogate and clinical outcomes with early abciximab use. In the study by Ortolani et al. [19], after adjustment for potential confounders, early administration was associated with favourable outcome in the overall population but especially in high-risk subgroups (TIMI risk index > 25, HR = 0.64, p = 0.02; Killip class > 1, HR = 0.54, p = 0.01). This might explain the differences between EUROTRANSFER Registry and the FINESSE study, where outcome after abciximab administration is very likely associated with risk profiles of patients [14, 21].

Results of this analysis also confirm that even in high experienced centres with well-organised STEMI hospital networks, time delays in STEMI patients from first medical contact until pPCI are still substantial, with only two in three patients receiving adequate treatment within 120 minutes. These results, similar to other national and international registries, support the idea of a pharmaco-invasive approach in patients with prolonged transfer times.

Limitations of the study

EUROTRANSFER has all the limitations of the registry study. One year follow-up data was gathered only with regard to mortality, and mostly by telephone calls. On the other hand, it is worth noting that as much as 93% of the patients completed follow-up.

CONCLUSIONS

Patients transferred for pPCI in STEMI hospital networks showed lower rates of death in long-term one-year clinical follow-up when treatment with abciximab was started early.

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Wczesne podanie abciximabu u pacjentów z zawałem serca z uniesieniem odcinka ST leczonych pierwotną przezskórną interwencją wieńcową poprawia rokowanie w obserwacji odległej. Dane z rejestru EUROTRANSFER

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Streszczenie

Wstęp: Pierwotna przezskórna interwencja wieńcowa (pPCI) jest preferowaną metodą reperfuzji mechanicznej u chorych z zawałem serca z uniesieniem odcinka ST (STEMI). Abciximab ma potwierdzoną skuteczność jako farmakologiczne leczenie wspomagające podczas pPCI. Nie jest jednak do końca jasne, kiedy podawać lek i czy jego wczesne zastosowanie wpływa na rokowanie. Istnieją rejestry, metanalizy i badania randomizowane, w których są prezentowane sprzeczne wyniki na temat optymalnego czasu podania abciximabu.

Metody: Do niniejszego rejestru włączono kolejnych chorych ze STEMI kierowanych do pPCI w sieciach współpracujących szpitali w leczeniu zawału serca w okresie od listopada 2005 do stycznia 2007 roku w 15 pracowniach kardiologii inwazyjnej w 7 krajach Europy. Zebrano dane dotyczące rocznej obserwacji klinicznej u 93% chorych.

Wyniki: W rejestrze EUROTRANSFER zebrano dane o 1650 pacjentach ze STEMI skierowanych do leczenia inwazyjnego. Abciximab zastosowano u 1086 chorych (66%). Wczesny abciximab (tzn. podany co najmniej 30 min przed pierwszym napełnieniem balonu w przypadku pPCI lub koronarografią w przypadku, gdy pPCI nie wykonywano) otrzymało 727 z nich (stworzyli grupę EA — *early abciximab*), natomiast 359 pacjentów otrzymało abciximab w pracowni kardiologii inwazyjnej (stworzyli grupę LA — *late abciximab*). W trakcie rocznej obserwacji zmarło 5,8% pacjentów z grupy EA i 10,3% z grupy LA ($p = 0,007$). Po wykonaniu przekształceń statystycznych (*propensity score*) w celu uniknięcia potencjalnej stronniczości danych związanej z charakterystyką wyjściową, wczesne podanie abciximabu (grupa EA) nadal wiązało się z mniejszym prawdopodobieństwem zgonu w okresie rocznej obserwacji odległej ($p = 0,004$). Zauważono także, że jedynie 36% chorych skierowanych do pracowni kardiologii inwazyjnej w rejestrze EUROTRANSFER zmieściło się w zalecanym przez europejskie wytyczne leczenia zawału serca oknie czasowym 90 minut od pierwszego kontaktu medycznego do leczenia zawału serca (PCI) i 60% dla okna 120 minut.

Wnioski: Pacjenci ze STEMI skierowani do leczenia inwazyjnego w sieciach współpracujących szpitali w leczeniu STEMI charakteryzują się mniejszą śmiertelnością w okresie obserwacji rocznej, jeśli abciximab był u nich zastosowany wcześnie.

Słowa kluczowe: zawał serca, przezskórna angioplastyka wieńcowa, abciximab, rejestr

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