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Outcome of thrombolysis in patients with acute myocardial infarction in rural Alberta

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[résumé]

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Abstract

Objective and method: To examine the use of thrombolytic agents in the treatment of acute myocardial infarction, the authors performed a chart review for 122 patients treated in 1992 in 36 of Alberta's 104 rural acute care hospitals with fewer than 100 beds. The outcome measures were death, complications of thrombolysis, transfer to referral centres and frequency of invasive procedures (angiography, angioplasty and bypass surgery). The standards of care were the percentage of patients with confirmed myocardial infarction, the time from presentation to thrombolysis and the use of ASA and ß-blockers.

Results: Eleven (9.0%) of the 122 patients died. Information about possible complications and investigations was unavailable for 1 of the patients. Of the remaining 121 patients, 62 (51.2%) had possible complications of thrombolysis, generally arrhythmias (in 32 [26.4%]), hypotension (in 28 [23.1%]) or minor bleeding (in 18 [14.9%]); 2 patients (1.7%) needed transfusion and 2

(1.7%) sustained cerebrovascular accidents. Of the total group of 122 patients, 72 (59.0%) were transferred to larger centres, one-third of these during the administration of thrombolytic agents. In 111 (91.0%) of the 122 patients myocardial infarction was confirmed. The average time from presentation to thrombolysis was 99.0 (range 19 to 410) minutes. Almost all of the patients received ASA (118 of 122 [96.7%]), and over half received ß-blockers (73 of 122 [59.8%]).

Conclusions: The physicians in these rural hospitals were using thrombolysis appropriately. The mortality and morbidity rates after thrombolysis were comparable to those in large urban studies, but there were delays in administering the thrombolytic agents.

Résumé

Objectif et méthode : Pour étudier l'utilisation d'agents thrombolytiques dans le traitement de l'infarctus aigu du myocarde, les auteurs ont effectué une étude rétrospective du dossier de 122 patients traités en 1992 dans 36 des 104 hôpitaux ruraux de soins actifs de l'Alberta comptant moins de 100 lits. Les mesures des résultats ont été les décès, les complications découlant de la thrombolyse, le transfert à des centres spécialisés et la fréquence des interventions effractives (angiographie, angioplastie et pontage chirurgical). Le pourcentage des patients victimes d'un infarctus du myocarde confirmé, la période écoulée entre la présentation et la thrombolyse et l'utilisation d'ASA et de bêta-bloquants ont constitué les soins normaux.

Résultats : Onze (9,0 %) des 122 patients sont morts. Les renseignements sur les complications possibles et les examens n'étaient pas disponibles dans le cas d'un des patients. Des 121 patients restants 62 (51,2 %) avaient des complications possibles découlant de la thrombolyse, en général des arythmies (32 [26,4 %]), de l'hypotension (28 [23,1 %]) ou un saignement mineur (18 [14,9 %]); 2 patients (1,7 %) ont eu besoin d'une transfusion et 2 autres (1,7 %) ont été victimes d'un accident cérébrovasculaire. Sur le groupe total de 122 patients, 72 (59,0 %) ont été transférés dans des centres plus importants, dont le tiers au cours de l'administration d'agents thrombolytiques. On a confirmé l'infarctus du myocarde chez 111 des 122 patients (91,0 %). La période moyenne écoulée entre la présentation et la thrombolyse s'est établie à 99.0 minutes (fourchette de 19 à 410 minutes). Presque tous les patients ont reçu de l'ASA (118/122 [96,7 %]) et plus de la moitié, des bêta-bloquants (73/122 [59,8 %]).

Conclusions : Les médecins de ces hôpitaux ruraux ont utilisé la thrombolyse comme il se doit. Les taux de mortalité et de morbidité après une thrombolyse étaient comparables à ceux qu'ont révélés d'importantes études en milieu urbain, mais il y a eu des retards dans l'administration des agents thrombolytiques.

Over the last 10 years the standard management of patients with acute myocardial infarction (MI) has changed considerably. Large, controlled trials have demonstrated that intravenous

thrombolysis reduces mortality from acute MI by about 18%.[1] Inevitably, such studies recruit patients from large or medium-sized hospitals equipped with coronary care units and specialist medical staff, and there is little information about the safety and efficacy of thrombolysis in rural hospitals staffed by family physicians. Only one Canadian study, in a large primary care hospital of 135 beds in Northern Ontario,[2] has examined this issue. Similarly, the use of adjunctive therapy consisting of ASA and ß-blocking agents, which also reduces mortality in acute MI,[3] has not been examined in rural areas.[4-6]

In the present study, a chart review, we examined the results of thrombolytic treatment in rural Alberta, where there are 104 acute care hospitals with fewer than 100 beds each, staffed almost exclusively by nonspecialist physicians. Over 80% of these hospitals provide thrombolytic treatment to patients with acute MI.[7] We wanted to determine whether thrombolysis is an appropriate treatment in a small hospital staffed by family physicians, each of whom can expect to see only one patient for thrombolysis in a year.8 In particular, we wanted to see if mortality and complication rates after thrombolysis were comparable to those in trials in other settings and if rural physicians were using thrombolysis and adjunctive agents effectively.

Methods

In 1993 we sent a questionnaire to senior physicians working in rural Alberta hospitals requesting information about the use of thrombolysis. Physicians from 104 hospitals were surveyed.[7] The questionnaire invited every hospital that provided thrombolytic therapy to participate in a chart review. Medical records staff at each hospital that agreed to participate identified the records of every patient who received thrombolytic therapy in 1992. They copied the complete chart for that admission and attached a copy of the discharge summary. If the patient had been transferred to another hospital, a copy of the discharge summary from the referral centre was also included. Confidentiality was maintained by removing identifying details about the patient and the treating physician. Each patient was assigned a code number by the local medical records staff, who entered this number on each copied document. The participating hospitals then forwarded the records to us for analysis. In addition, hospital staff completed a short questionnaire about the facility. Ethical approval for the study was granted by the Ethics Review Committee of the Faculty of Medicine, University of Alberta, Edmonton.

We extracted baseline information about the patients, such as age, sex, history of previous MI and site of current infarction. To determine standards of care we recorded time from presentation to thrombolysis, use of ASA and ß-blockers (as recorded in the charts of either the rural or referral hospital) and whether MI was confirmed. The time from presentation to thrombolysis was calculated only for patients who had clear indications for thrombolysis at presentation. For example, this elapsed time was not calculated for patients initially presenting with nondiagnostic electrocardiography results who subsequently fulfilled the criteria for thrombolysis.

A case was classified as confirmed MI if at least two of the following criteria were present: chest

pain, electrocardiographic changes consistent with acute MI or an increase in cardiac enzymes (specifically creatinine kinase). If only one of the criteria was present and the discharge diagnosis on the chart was probable or possible MI, the case was classified as probable/possible MI. Other events were classified as definitely not MI.

We also collected outcome data concerning deaths during hospital stay, complications of thrombolysis, transfers and length of stay. Adverse events, such as bleeding, cerebrovascular accident, arrhythmia, hypotension or allergic reactions, occurring within 2 hours of completion of the thrombolytic infusion were recorded as possible complications. However, for bleeding complications (including cerebrovascular accident) the time limit was extended to 24 hours. Bleeding that necessitated transfusion was defined as major bleeding; all other bleeding was classified as minor.

The data were analysed with Epi-Info 5 software[9] and SPSS, version 6.0. When applicable, the data were tested for statistical significance with Student's t-test or the chi2 test.

Results

Eighty-four of the 104 hospitals were providing thrombolytic treatment at the time of the survey, and 39 of these hospitals agreed to participate in the study. Of the 130 charts that we received, we excluded 7 because of missing and unobtainable data and 1 because there was no record of the patient receiving thrombolytic agents. Thus, 122 records from 36 hospitals remained for analysis (mean 3.4 patients per hospital, standard deviation [SD] 2.8). The mean number of acute care beds in these hospitals was 36.0 (SD 14.1). The mean distance from the nearest referral centre was 213.4 (SD 154.5) km, and the average number of medical staff was 5.9 (SD 3.6). None of these hospitals had internists on their regular medical staff.

Table 1 presents demographic information about the 122 patients who received thrombolysis. Most of the patients received streptokinase (84 of 122 [68.9%]), and the remainder received tissue plasminogen activator. MI was confirmed in 111 of the 122 patients (91.0%). In 4 of the 122 patients (3.3%) the diagnosis was possible or probable MI, and in 7 (5.7%) it was definitely not MI.

The mean time from presentation to the start of thrombolysis ("door-to-needle" time) in the 104 patients in whom there were clear indications for thrombolysis at presentation was 99.0 (SD 65.6, range 19 to 410) minutes. Thrombolysis was started within 1 hour of arrival at the hospital in only 27 (26.0%) of these patients; however, thrombolysis was started within 2 hours for 80 (76.9%).

ASA was given to almost all (118 [96.7%]) of the 122 patients at some point during their hospital stay. Adjunctive therapy with ß-blockers had been recorded in 73 (59.8%) of the 122 patients.

Table 2 summarizes the overall outcomes for patients who received thrombolytic agents. The final outcome was not known for 2 of the patients who were referred for angioplasty, and information about possible complications and investigations was missing for 1 patient. Ten of the 11 deaths were directly related to MI: 8 were due to cardiogenic shock, 1 occurred after attempted repair of the interventricular septum, and 1 patient suffered sudden cardiac death while awaiting surgery in the referral centre. The other death was due to a cerebrovascular accident. The mean time from thrombolysis to death was 1.4 (range 0 to 5) days, and 5 patients died on the day of thrombolysis. Four patients died in rural hospitals, 6 in referral centres and 1 en route to a referral centre.

Potentially avoidable circumstances were judged to be present in only 2 instances. Despite clear indications, thrombolysis was not started for 200 minutes in 1 of the patients. In another case third-degree heart block and cardiogenic shock developed, and assistance was requested promptly. Despite this request for assistance, a further 3 hours elapsed before a team from the nearest tertiary care centre arrived. Asystole developed a few minutes after the team's arrival. The time to travel between the two hospitals is about 1 hour by helicopter and 2 hours by ground ambulance.

Adverse events occurring after thrombolysis are detailed in Table 3. The most frequent of these were arrhythmias (Table 4). Four patients experienced cardiac arrest within 2 hours after undergoing thrombolysis. An additional 7 patients had episodes of ventricular fibrillation before treatment with thrombolytic agents.

Other common complications were hypotensive episodes and minor bleeding. Hypotension was more common in patients who received streptokinase (23 [27.4%] of 84) than in patients who received tissue plasminogen activator (5 [13.5%] of 37), but this difference was not statistically significant (chi2 test, $p = 0.08$). One patient experienced a mild allergic rash after receiving streptokinase.

The thrombolytic infusion was not completed in 10 patients. Three died during thrombolysis, 4 experienced severe hypotension (all 4 of whom had been treated with streptokinase), and in 2 patients there were problems with leakage from the intravenous access site. The infusion was stopped in the 10th patient because of hematemesis.

Twenty-four (33.3%) of the 72 patients transferred to another centre were transported during the thrombolytic infusion, and a further 11 (15.3%) were moved within an hour of completion of the infusion. The mean length of stay from admission to discharge was 9.9 days.

Discussion

The results of this study suggest that these rural hospitals were using thrombolytic therapy for

acute MI effectively, despite the infrequency of use (less than 1 case per physician annually). The mortality rate of 9.0% is comparable to that after fibrinolysis (9.6%), as reported in a meta-analysis of large trials.1 The same meta-analysis reviewed complications and reported the frequency of stroke as 1.2% and of major noncerebral bleeding as 1.1%; we observed a rate of 1.7% for both events. At first glance, the use of thrombolytic agents in cases in which MI was not confirmed (11 [9%] of 122 cases) appears worrisome. However, this result accords with calculations presented in a Swedish study,10 in which the authors suggested that MI would be confirmed in 91% of patients presenting within 6 hours of initial chest pain if ST segment elevation was present on the electrocardiogram. This theoretical rate of use of thrombolysis was borne out by the trial of the European Myocardial Infarction Project Group involving prehospital therapy by mobile emergency physicians; in that study the rate of confirmed MI was 87.6%.[11]

The rate of ASA use in our study (97.6%) is comparable to the rates of 71%[5] and 95%[6] previously reported for Canada. The rate of use of ß-blockers (59.8%) is higher than published rates of 38% in a large US review[4] and 31% in a Canadian urban study,[5] although the latter 2 figures apply to all patients treated for acute MI, not just the subgroup treated with thrombolytic agents. However, in another study at a large Canadian hospital ß-blockers were used in almost 75% of patients with acute MI.[6] This suggests that some eligible patients in our study did not receive ß-blockers.

Our previous study[7] showed that some rural physicians were concerned that the complication rate for thrombolysis was too high for this treatment to be used in rural hospitals. Although more than half of the patients in the current study had possible complications of thrombolysis, many of these were of little clinical significance. Serious complications other than arrhythmias were uncommon, occurring in only 8 (6.6%) of 121 patients. Two patients needed transfusion, 2 suffered cerebrovascular accidents, and 4 had such profound hypotension that the thrombolytic regimen could not be completed. Although arrhythmias occurred frequently, it is likely that they were associated with the cardiac event rather than the thrombolysis. Pooled data from the large trials of thrombolytic agents suggest that the risk of ventricular fibrillation is reduced by thrombolysis.[12] It is interesting that the classic reperfusion arrhythmia, accelerated idioventricular rhythm, was only documented once in our study.

We were also interested in how quickly rural hospitals could mobilize to provide thrombolytic therapy. Several studies have examined this issue in urban hospitals, demonstrating that there can be a marked delay between presentation at the hospital and initiation of thrombolysis.[13-15] Although thrombolysis is beneficial even when given up to 12 hours after the onset of chest pain, maximal benefit accrues if treatment is started early.[1]

Recent guidelines recommend a target time of 30 minutes from presentation to initiation of thrombolysis.16 In this study the mean time to thrombolysis was 99 minutes, with only a quarter of patients starting the thrombolytic therapy within the first hour. The reasons for this delay in providing treatment are speculative but may include the need to call in the physician from home

or office, a requirement in some hospitals for consultation with a second physician and the necessity to obtain extra nursing staff to perform the infusion. Whatever the reasons, it is apparent that there is room for improvement in this area. Reports suggest that "door-to-needle" time can be shortened in urban hospitals by the use of check-lists of contraindications, abbreviated clinical assessments and initiation of treatment in the emergency department,[13-15] but it is not clear that these measures would be applicable in small rural facilities.

This study was limited because of its retrospective nature, a limitation that was compounded by the difficulties inherent in dealing with a large number of participating sites and not having access to the entire chart for patients transferred to referral centres. In large trials mortality rates are usually calculated up to day 35, but we were able to calculate mortality only up to the date of hospital discharge. We cannot be sure that the participating hospitals identified every case of thrombolysis, as medical record coding for this procedure is not mandatory. Some minor complications such as insignificant bruising may have escaped documentation. In addition, it is important to be aware that these results are not necessarily representative of practice in rural Alberta, since fewer than half of the hospitals using thrombolytic agents participated. However, data from our previous study[7] suggest that the characteristics of the study group of 36 hospitals are similar to those of all of the 84 rural hospitals providing thrombolysis at that time. That larger group of hospitals had a mean number of beds of 37.7, a mean number of medical staff of 5.5 and a mean distance from a referral centre of 172.9 km.

Despite these limitations our study has implications for current practice in rural hospitals. We need to ensure that eligible patients receive thrombolysis more promptly, and we need to encourage more widespread use of ß-blockers. Physicians also need to examine transfer policies with care. In this study most patients were transferred to larger centres, frequently during the thrombolytic infusion. However, there are risks associated with immediate transfer, given the high prevalence of hypotension during thrombolysis and the frequency of malignant arrhythmias in the first hours after acute MI. Accordingly, high-level resuscitation skills must be available during transfer. A number of trials have demonstrated the safety of prehospital thrombolysis administered by specially trained teams.[11,17] These reassuring results are not necessarily applicable to rural Canada, where it may sometimes be appropriate to delay transfer until after the thrombolytic infusion is complete. Conversely, delay in transferring high-risk patients, who may benefit from specialist care and access to revascularization, should be avoided.

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