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CLINICAL RESEARCH

Door-to-balloon delays before primary angioplasty in the Regional Acute Myocardial Infarction Registry of Brittany. An analysis of the *Observatoire Régional Breton sur l'Infarctus du myocarde* (ORBI)

Délais de prise en charge de l'infarctus ST+ traité par angioplastie primaire en Bretagne. Une analyse de l'observatoire régional breton sur l'infarctus du myocarde (ORBI)

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Abbreviations: ACS, acute coronary syndrome; EMS, emergency medical services; AMI, acute myocardial infarction; ORBI, Observatoire Régional Breton sur l'Infarctus.

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KEYWORDS

Acute myocardial infarction;
Primary angioplasty;
Emergency medical services;
First aid;
Transportation of patients

Summary

Background. — Minimizing delays to coronary reperfusion is critical in the management of acute myocardial infarction (AMI).

Aims. — To determine delays in in-hospital management and factors associated with delays of over 45 min.

Methods. — We analysed data from the Observatoire Régional Breton sur l'Infarctus, a registry of AMI patients admitted within 24 h of symptom onset (July 2007 to December 2008) to an interventional cardiology centre in Brittany. Prehospital delay was defined as time between first responder arrival at the patient and patient arrival at an interventional cardiovascular centre. In-hospital delay was defined as time between admission to the interventional cardiovascular centre and first balloon inflation. Patients were grouped according to duration of in-hospital delay (>45 vs ≤45 min). Predictors of short in-hospital delay (≤45 min) were examined by logistic regression analysis.

Results. — The analysis included 560 patients (mean age 60.7 ± 13 years; 443 men). Median delay between symptom onset and call for medical assistance was 50 min (mean 115 ± 180). Two-thirds (n = 371) of patients were admitted to hospital during working hours (08:00–20:00 h); 383 (68%) patients were managed by emergency medical services before admission. In-hospital delay was less than or equal to 45 min for 296 (53%) patients. The mean overall (pre- and in-hospital) delay was 140 (median 109) min. Direct admission to a catheterization laboratory and admission during working hours were independently correlated with short in-hospital delay (odds ratios 20.8 [*p* < 0.001] and 2.37 [*p* = 0.004], respectively).

Conclusions. — In Brittany, median in-hospital delay before treatment of AMI by primary angioplasty was over 45 min in 50% of patients. Overall, delays were longer than recommended, due to excessively long prehospital delays. Patient admission during working hours and direct admission to a catheterization laboratory were associated with short in-hospital delay.

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MOTS CLÉS

Infarctus aigu du myocarde ;
Angioplastie primaire ;
Service d'aide médicalisée d'urgence ;
Premier contact ;
Transports des patients

Résumé

Justification. — La réduction des délais de reperfusion coronaire est particulièrement importante pour l'efficacité de l'angioplastie primaire, à la phase aiguë de l'infarctus du myocarde.

Objectifs. — Déterminer (1) les délais de prise en charge intrahospitaliers, (2) les facteurs prédictifs d'un délai intrahospitalier inférieur ou égal à 45 min, (3) les mesures permettant de réduire ces délais.

Méthodes. — Nous avons analysé les données colligées dans l'observatoire régional breton sur l'infarctus (ORBI) de tous les patients hospitalisés entre le 1^{er} juillet 2007 et le 31 décembre 2008 pour prise en charge d'un infarctus du myocarde de moins de 24 heures dans un centre d'angioplastie breton, traités par angioplastie primaire. Le délai préhospitalier était défini comme le délai entre le premier contact médical et l'admission du patient dans le centre de cardiologie interventionnelle. Le délai intrahospitalier était défini comme le délai entre cette admission et la première inflation du ballon d'angioplastie. Les patients étaient séparés en deux groupes, selon que le délai intrahospitalier était supérieur à 45 ou inférieur à 45 minutes. Les facteurs prédictifs d'un délai intrahospitalier inférieur ou égal à 45 minutes ont été recherchés à l'aide d'une analyse par régression logistique.

Résultats. — L'analyse a porté sur 560 patients (âge moyen = 60,7 ± 13 ans, 443 hommes). Le délai médian entre le début des symptômes et le premier appel était de 50 minutes (moyenne : 115 ± 180). La prise en charge était comprise entre 08:00 h et 20:00 h chez 371 patients (66%) et 383 patients (68%) ont été pris en charge par le Samu avant l'admission. Le délai intrahospitalier était inférieur ou égal à 45 minutes pour 296 patients (53%). Le délai total

(pre- + intrahospitalier) moyen était de 140 minutes, et médian de 109 minutes. L'analyse multivariée montre que: (1) l'admission directe en salle de cathétérisme et (2) la survenue des symptômes entre 08:00 h et 20:00 h, sont les seuls facteurs prédictifs d'un délai intrahospitalier inférieur à 45 min, avec des odds ratios de 20,8 ($p < 0,001$) et 2,37 ($p = 0,004$), respectivement. *Conclusion.* – En Bretagne, le délai médian intrahospitalier avant reperfusion des infarctus aigus traités par angioplastie primaire est supérieur à 45 minutes chez 50% des patients. Les délais de prise en charge supérieurs aux recommandations sont aussi le fait de délais préhospitaliers trop longs. Une admission entre 08:00 h et 20:00 h, ainsi qu'une admission directe en salle de cathétérisme sont les seuls facteurs prédictifs d'un délai intrahospitalier inférieur ou égal à 45 minutes.

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Background

Primary angioplasty is the reperfusion method of choice for the initial management of patients presenting with AMI and persistent ST-segment elevation, provided that the delays preceding their admission and the onset of therapy are within the limits recommended by current guidelines [1]. European [2] and North American [3] professional guidelines both recommend a maximum delay of 90 min between the first medical contact and balloon inflation [4–8]. This 90-min delay can be divided between the time elapsed between the first medical contact and arrival at an interventional cardiology centre (prehospital delay), and the time elapsed between arrival at the centre and first inflation of the angioplasty balloon (in-hospital delay). Experts participating in the consensus conference on the management of AMI outside of cardiology centres chose 45 min as the 'decision threshold' for the delay between first medical contact and admission to an interventional cardiology centre, based on an estimated in-hospital delay of 33–45 min [9]. The aim of this study was to determine precisely the actual delays in in-hospital management, based on the Regional Acute Myocardial Infarction Registry of Brittany, the factors associated with delays over 45 min and the methods or management measures that might shorten these delays.

Methods

This observational study was based on data collected by the ORBI, a registry that includes prospectively all patients admitted within 24 h of onset of symptoms to an interventional cardiology centre in Brittany (participating centres are listed in the Acknowledgements) with a final diagnosis of ACS with persistent ST-segment elevation. We studied all patients included in the ORBI registry who underwent primary angioplasty between 1st July 2007 and 31 December 2008. Patients were excluded if they were treated with fibrinolysis, admitted to another hospital before being transferred to an interventional cardiology centre or did not undergo primary angioplasty. Prehospital delay was defined as the time elapsed between the arrival at the patient of the first physician who made the diagnosis and the arrival of the patient at an interventional cardiovascular centre. Therefore, this delay applied only to patients who were managed medically before their admission to the hospital.

In-hospital delay was defined as the time elapsed between the patient's admission to the interventional cardiovascular centre (whether to the emergency department, the intensive care unit or directly to the catheterization laboratory) and the first angioplasty balloon inflation (or thrombectomy, if applicable). All demographic, electrocardiographic and timing data were collected prospectively.

Statistical analyses

Quantitative data are expressed as means \pm standard deviations and qualitative data as counts and percentages. A delay of 45 min was chosen as the 'threshold' and patients were grouped according to whether they experienced an in-hospital delay of more than 45 or less than or equal 45 min. Between-group comparisons were made using Student's *t*-test (or Wilcoxon's test, as appropriate) for quantitative variables and the χ^2 test for qualitative variables. Factors found to have a significant influence by univariate analysis at a *p* level of 0.05 were included in a multivariable logistic regression analysis. All analyses were performed using the SAS® Version 9.1 statistical package (SAS Institute Inc., Cary, NC, USA). A *p*-value < 0.05 was considered to be statistically significant.

Results

Study population

The overall study population comprised 560 patients. Among the eight participating medical centres, two included more than 100 patients (a total of 290 patients), two included 50–100 patients (a total of 144 patients) and four included less than 50 patients (a total of 126 patients). Important patient and treatment characteristics are listed in Table 1. The mean age of the 443 men and 117 women was 60.7 ± 13 years. Hypertension was present in 206 (37%) patients, diabetes in 58 (10%) patients, hypercholesterolaemia in 269 (48%) patients, family history of coronary artery disease in 142 (26%) patients and 228 (41%) patients were current smokers. The area of myocardial infarction was anterior in 246 (44%) patients.

First response

ACS was the first manifestation of coronary artery disease in 444 (79%) patients. The median delay between onset of

Table 1 Predictors of in-hospital delay by univariate and multivariable logistic regression analyses.

| Variable | In-hospital delay | | Analysis | | Odds ratio |
|--|-------------------|-----------|------------|-------------------|-----------------------------|
| | ≤ 45 min | > 45 min | Univariate | Multivariable | |
| | (n = 296) | (n = 264) | p | p | |
| Age (years) | 59.9 ± 13 | 61.7 ± 14 | 0.12 | — | — |
| Men | 245 (83) | 198 (75) | 0.024 | 0.54 | 0.76 [0.3–1.8] |
| Delay (min) | | | | | |
| Symptom to first call | 87 ± 126 | 160 ± 233 | < 0.001 | 0.12 | 0.99 [0.9–1.0] |
| Prehospital | 73 ± 36 | 81 ± 57 | 0.59 | — | — |
| Initial event | | | 0.62 | — | — |
| Present | 237 (80) | 207 (78) | | | |
| Absent | 59 (20) | 57 (22) | | | |
| Delivery of care | | | 0.012 | 0.004 | 2.37 [1.1–4.7] |
| Between 08:00 and 20:00 h | 210 (71) | 161 (61) | | | |
| Between 20:01 and 07.59 h | 86 (29) | 103 (39) | | | |
| Prehospital care by emergency medical service | | | < 0.001 | 0.09 | 0.71 [0.2–1.9] |
| Present | 277 (96) | 106 (40) | | | |
| Absent | 19 (4) | 158 (60) | | | |
| Site of patient admission | | | < 0.001 | < 0.001 | 20.8 [8.6–50.7] |
| Catheterization laboratory | 269 (91) | 43 (16) | | | |
| Emergency intensive cardiac unit | 27 (9) | 221 (84) | | | |
| First intervention | | | < 0.001 | 0.17 ^a | 0.57 [0.2–1.2] ^a |
| Emergency medical services | 138 (47) | 64 (24) | | | |
| General practitioner | 74 (25) | 67 (25) | | | |
| Urban cardiologist | 3 (1) | 0 | | | |
| No prehospital care | 28 (9) | 69 (26) | | | |
| Missing data | 53 (18) | 64 (25) | | | |
| Number of patients contributed by participating centre | | | 0.52 | — | — |
| < 50 | 68 (23) | 58 (22) | | | |
| Between 50 and 100 | 82 (27) | 62 (23) | | | |
| > 100 | 146 (50) | 144 (55) | | | |
| Area of infarction | | | 0.61 | — | — |
| Anterior | 133 (45) | 113 (43) | | | |
| Non-anterior | 163 (55) | 151 (57) | | | |
| Presence of Q wave on admission electrocardiogram | | | 0.11 | — | — |
| Yes | 106 (36) | 115 (43) | | | |
| No | 190 (64) | 149 (57) | | | |

Data are mean ± standard deviation for quantitative variables and count (%) for qualitative variables.

^a Emergency medical services vs other contact.

symptoms and call for medical assistance was 50 min, and the mean delay was 115 ± 180 min.

First medical intervention

No prehospital care was delivered to 97 (17%) patients. The first medical intervention for the 463 remaining patients was offered by EMS or ambulance-based physicians (202 [36%] patients), by a general practitioner/family physician (141 [25%] patients) or and by urban cardiologists (three

[0.5%] patients) (Table 1). These data were missing for 117 (20%) patients. First aid was delivered during working hours (between 08:00 and 20:00 h) to 371 (66%) patients; 383 (68%) patients were managed by EMS before admission to the hospital.

Patient admission to hospital

The catheterization laboratory was the site of admission for 312 (56%) patients, the emergency department or triage

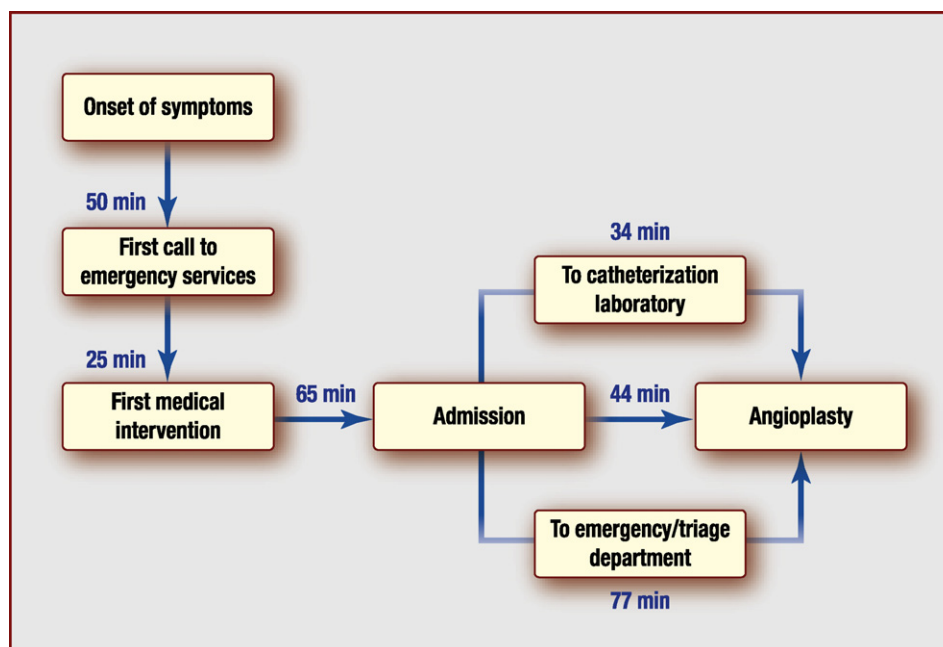


Figure 1. Median management delays.

centre for 144 (26%) patients and the intensive care unit for 104 (18%) patients.

Management delays

The pre- and in-hospital delays are illustrated in Fig. 1. The mean prehospital delay was 76 ± 44 min and the median delay was 65 min. The mean in-hospital delay was 64 ± 66 min and the median delay was 44 min. The in-hospital delay was less than or equal to 45 min for 296 (53%) patients. The mean overall (pre- and in-hospital) delay was 140 min and the median delay was 109 min. The overall delay before onset of balloon inflation was less than or equal to 90 min in only 193 (35%) patients.

Predictors of in-hospital management delays by logistic regression analysis are shown in Table 1. By univariate analysis, the following factors were associated significantly with an in-hospital delay of less than or equal to 45 min: male sex; short delay between onset of symptoms and first call; onset of care during working hours; prehospital care by EMS; direct admission to the catheterization laboratory; and the type of first patient contact. By multivariable analysis, the only factors that correlated significantly with an in-hospital delay of less than or equal to 45 min were direct admission to the catheterization laboratory (odds ratio 20.8, $p < 0.001$) and onset of care during working hours (odds ratio 2.37, $p = 0.004$). In 312 patients who were admitted directly to the catheterization laboratory, the median in-hospital delay was 34 min, in contrast with 77 min in 248 patients who were admitted elsewhere. The median delay was 40 min in 371 patients admitted during working hours versus 51 min in 189 patients admitted outside of working hours.

Finally, no difference was observed among the participating centres with respect to the number of patients treated, with median delays of 45, 40 and 46 min in centres that included less than 50, 50–100 and more than 100 patients, respectively.

Discussion

The results from the ORBI registry confirmed that the delay between first medical intervention and first balloon inflation in clinical practice was longer than the recommended 90 min in over 60% of patients. Even when prehospital factors were contributors to the postponement of onset of care, the in-hospital delays remained longer than recommended in nearly 50% of patients.

Delays in onset of care

The median in-hospital delay was 44 min, within the limits recommended by professional guidelines [9]. Comparisons with previous studies are problematic because the delay most often reported is 'door-to-balloon', and variability in the organization of healthcare between countries means that the definition of this delay is ambiguous. It is defined, in non-French publications, as the interval between hospital admission and angioplasty balloon inflation, whereas in reports of French studies it is defined as the interval between first medical contact and balloon inflation [9]. With the support of the Haute Autorité de santé, French-speaking societies of emergency medicine and the French EMS proposed to divide the 'door-to-balloon' delay between 'door-to-cardiology door' (corresponding to our definition of prehospital delay) and 'cardiology door-to-balloon' (corresponding to our definition of in-hospital delay), associated with a 45-min threshold [9]. In the E-MUST registry, which included 1085 patients treated with primary angioplasty [10], the median 'cardiology door-to-introduction of angioplasty wire' delay of 36 min was shorter than that observed in our study. Furthermore, in our analysis, the overall delay associated with initial management (i.e., pre- and in-hospital delays, corresponding to the 'door-to-balloon' delay of professional guidelines) was unsatisfactory, as it was less than or equal to 90 min in only one-third of

patients, with a median value of 109 min. This was due in part to a long prehospital ('door-to-cardiology door') delay. The various French registries of management of AMI have reported different median 'door-to-balloon' delays, depending on the region they encompassed, ranging from 81 min in the 1330 patients of E-MUST, organised by the EMS of metropolitan Paris [10], to 150 min in RESURCOR, in which 75% of patients were treated with primary angioplasty [11], and 157 min in the ALSACE registry, which included 244 patients [8]. Data from the United States are not superior: in the National Registry of Myocardial Infarction, conducted between 1999 and 2002, only 35% of patients were treated within 90 min of admission to hospital and less than 15% of hospitals recorded median delays of less than 90 min [12]. On the other hand, in the National Registry of Myocardial Infarction-4, which included 21,277 patients presenting with AMI treated with primary angioplasty [13], the median 'door-to-balloon' delay was 83.9 min when an electrocardiogram was recorded before admission versus 107.7 min when no electrocardiogram was recorded.

The European Society of Cardiology has issued new guidelines recently regarding the management of ST-segment elevation myocardial infarction [14]. The maximal delay recommended between first medical contact and inflation of the angioplasty balloon is 120 min. However, with respect to the initial choice of mode of revascularization, the authors specify that when patients present within less than 2 h, with a low risk of haemorrhage or a large area of infarction, the delay should be less than 90 min.

Methods of shortening in-hospital delay

Our analysis shows the importance of direct admission of the patient to the catheterization laboratory, without transit through other services, such as triage or emergency departments, or cardiology intensive care. In this study, only 56% of patients who underwent primary angioplasty were admitted directly to the catheterization laboratory. In the French national registry FAST-MI, which included 566 patients presenting with AMI treated with primary angioplasty, 40.3% of patients were admitted directly to the catheterization laboratory [15]. In the E-must registry [10], 83.5% of patients were admitted directly to the catheterization laboratory when an initial decision was made in 330 patients to proceed with primary angioplasty. That registry also highlighted the 'adverse' consequences of the transit of patients through a cardiology intensive care unit, which delayed the performance of coronary angiography by a mean 38 min, particularly during the night.

A study from the United States examined various treatment strategies among 365 hospitals, with respect to shortening the 'door-to-balloon' delay (median 100.4 min) [16]. A significant shortening of the delay was associated with six strategies:

- the presence of an intensivist, who activates the catheterization laboratory without intervention from a cardiologist (shortening the delay by 8.2 min);
- the availability of a telephone contact person, who alerts the interventional cardiologist and the catheterization laboratory (shortening of 13.8 min);

- the existence of EMS, which activate the catheterization laboratory during transfer of the patient (shortening of 15.4 min);
- the ability of catheterization staff to be in the laboratory within 20 min of being called (shortening of 19.3 min);
- the permanent on-site presence of a cardiologist (shortening of 14.6 min);
- the real-time transfer of information between the emergency service staff and the catheterization laboratory (shortening of 8.6 min).

These strategic measures are, for the most part, already implemented in France, as opposed to the direct admission of patients to the catheterization laboratory, which, in our analysis, shortened the in-hospital delay by 43 min.

A study from Germany, which included a small number of patients, examined the benefits conferred by changing usual practice, and by admitting 74 patients presenting with ST-segment elevation myocardial infarction directly to the catheterization laboratory versus 63 matched patients treated conventionally, including transit through a triage or emergency department [17]. The median 'door-to-balloon' time was 89 min for the group admitted directly to the catheterization laboratory versus 118 min for the group treated conventionally ($p=0.001$). A study from Australia found that the recording of an electrocardiogram before admission to the hospital, with a view to directing the patient immediately to the catheterization laboratory, allowed a significant shortening of pretreatment delays and lowering of blood creatine kinase concentration and mortality [18]. Finally, in a recent study of 577 patients, which confirmed the merits of admitting the patients to the catheterization laboratory directly, the median 'door-to-balloon' delay was 58 min, compared with 105 min for patients who transited through the emergency department ($p<0.001$) [19].

Direct admission of patients to the catheterization laboratory requires the delivery of prehospital care by EMS. In the RICO registry, which included 531 patients, the mean 'door-to-cardiology door' time, i.e., the prehospital delay, was shortened from 90 to 59 min ($p<0.05$) when EMS or fire-fighters delivered prehospital care [20]. In addition, the time of day had an influence on the delay to onset of coronary reperfusion. Patient management outside working hours, at night, lengthened the delays, as reported previously [21–23]. In the National Registry of Myocardial Infarction, the median 'door-to-balloon' time, measured in nearly 34,000 patients between 1999 and 2002, was significantly longer when care had to be delivered outside working hours (116 min) compared with during (95 min) working hours [24]. Finally, in our study, and in contrast with previous reports of a more expeditious delivery of care by 'high-volume' medical centres [25], the number of patients contributed by each centre was not a predictor of intrahospital delay.

Study limitations

While the ORBI registry data, particularly the times of call and onset of patient management, were collected meticulously, the information gathered at each participating medical centre was not monitored independently. Further-

more, the influence on in-hospital delays of femoral versus radial arterial catheterization access and the operator's experience were not examined.

Conclusions

In Brittany, the median in-hospital delay before the onset of treatment of ACS with persistent ST-segment elevation by primary angioplasty was nearly 45 min, i.e., the delay was greater than 45 min in 50% of patients. Overall, the delays were longer than recommended also, due to excessively long prehospital delays. Admission of the patient between 08:00 and 20:00 h and direct admission to a catheterization laboratory without transit through a triage or emergency department were the only independent predictors of an in-hospital delay less than or equal to 45 min. A strategy based on direct calls by patients to a central service, pre-hospital care initiated by an emergency team and direct admission of the patients to a catheterization laboratory is the only means of shortening these delays toward values recommended by professional guidelines for the management of ACS by primary angioplasty.

Conflicts of interest

None.

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The following medical centres participated in this study: CHU de Rennes; clinique Saint-Laurent, Rennes; CHU de Brest; centre hospitalier de St. Malo; centre hospitalier de St. Briec; centre hospitalier de Lorient; centre hospitalier de Vannes, centre hospitalier de Quimper.

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