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The transtelephonic electrocardiogram-based triage is an independent predictor of decreased hospital mortality in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention

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Abstract

Introduction: The transtelephonic electrocardiogram has been shown to have a great value in the management of out-of-hospital chest pain emergencies. In our previous study it not only improved the pre-hospital medical therapy and time to intervention, but also the in-hospital mortality in ST-segment elevation myocardial infarction. It was hypothesised that the higher in-hospital survival rate could be due to improved transtelephonic electrocardiogram-based pre-hospital management (electrocardiogram interpretation and teleconsultation) and consequently, better coronary perfusion of patients at the time of hospital admission. To test this hypothesis, our database of ST-segment elevation myocardial infarction patients was evaluated retrospectively for predictors (including transtelephonic electrocardiogram) that may influence in-hospital survival.

Methods and results: The ST-segment elevation myocardial infarction patients were divided into two groups, namely (a) hospital death patients ($n = 49$) and (b) hospital survivors (control, $n = 726$). Regarding pre-hospital medical management, the transtelephonic electrocardiogram-based triage (odds ratio 0.48, confidence interval 0.25–0.92, $p = 0.0261$) and the administration of optimal pre-hospital medical therapy (acetylsalicylic acid and/or clopidogrel and glycoprotein IIb/IIIa inhibitor) were the most important independent predictors for a decreased risk in our model. At the same time, age, acute heart failure (Killip class >2), successful pre-hospital resuscitation and total occlusion of the infarct-related coronary artery before percutaneous coronary intervention were the most important independent predictors for an increased risk of in-hospital mortality.

Discussion: In ST-segment elevation myocardial infarction patients, (a) an early transtelephonic electrocardiogram-based teleconsultation and triage, (b) optimal pre-hospital antithrombotic medical therapy and (c) the patency and better perfusion of the infarct-related coronary artery on hospital admission are important predictors of a lower in-hospital mortality rate.

Keywords

Remote consultation, telecardiology, teleconsulting, telemedicine

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Introduction

Ischaemic heart disease is one of the leading causes of death worldwide. In the case of ST-segment elevation myocardial infarction (STEMI), mortality in the first six months may exceed 10%.[1] In the case of STEMI, an early diagnosis and the prevention of any delay are critical for an improved outcome. The earlier the treatment, the greater the benefit, i.e. 'time is muscle'. In the majority of STEMI cases the first medical contact takes place outside the hospital setting, usually by the paramedic staff.[2] This is why the primary, pre-hospital diagnosis of STEMI and the initiated therapy are generally based on the typical signs/symptoms of the disease and especially on the electrocardiogram (ECG), as biomarker measurements are usually not readily available. Besides the traditional pre-hospital 12-lead ECG, the transtelephonic ECG (TTECG) can also be used by the paramedics. This system has already been shown to be of beneficial value in the diagnosis of ischemic heart disease and in the management of out-of-hospital chest pain emergencies.[2] In our previous study, we demonstrated that the utilization of TTECG and TTECG-based consultation between paramedics and specialists has significantly improved: (a) pre-hospital medical therapy, (b) time-to-percutaneous coronary intervention (PCI) and (c) in-hospital mortality in a large patient cohort ($n = 775$) with STEMI.[3] Then we hypothesised that the higher in-hospital survival rate could be due, at least in part, to a TTECG-based early diagnosis that significantly improves pre-hospital medical therapy and results in better coronary artery perfusion of patients at the time of hospital admission.[3]

To test this hypothesis, we decided to retrospectively evaluate our database of STEMI patients ($n = 775$) for: (a) TTECG procedures, (b) demographic factors, comorbidities and cardiac risk factors, (c) pre-hospital medical therapy and (d) coronary artery patency and flow before primary PCI. In particular, we chose to determine the various predictors among pre-hospital management data (including TTECG) and PCI procedural findings that may influence the in-hospital survival of patients. Our objective was to investigate the difference between the hospital death group and hospital survival group (control) in an anticipation that an early TTECG and the TTECG-based pre-hospital therapy of the STEMI patients would translate into better coronary flow on hospital admission and improved chance of patient survival.

Methods

Data collection

Patient selection and TTECG methodology were previously described in detail.[3] The STEMI patients were divided into two groups, namely (a) hospital death patients at day 20 ($n = 49$) and (b) hospital survivors (control, $n = 726$). TTECG was done with a battery-operated, 12-lead, portable system (HeartView P12/8 Plus by Aerotel). The data transmission was carried out via the radiotelephone system of the Hungarian National Ambulance Service (Tetra). The decision to obtain TTECG was based on the discretion of the paramedic group. Some teams obtained and transferred TTECG from all patients and other teams made it only if they had problems with the clinical diagnosis and/or with the interpretation of the ECG.[3] TTECG was used more frequently by the paramedics if the scene of the patients was more distant from the PCI centre (rural areas). After transmitting the ECG signal to the PCI centre, all important clinical data of the patient (including the ECG findings and possible pre-hospital medical therapy) and the patient's transport have been discussed in a short teleconsultation.

Acute heart failure (AHF) was defined as a Killip class >2 during the pre-hospital period. Coronary angiography investigations were performed by a Philips Integris CV device, and cine loops were recorded at 15 frames/s using 300 mg iodine/ml non-ionic contrast material. During the examination, intracoronary nitrate of 200 μg was administered to provide full vasodilatation. The primary PCI procedure was performed in the standard way.

The patency of the infarct-related artery (Thrombolysis in Myocardial Infarction (TIMI) grade) during catheterisation was visually assessed pre-PCI (during the first coronary angiogram of the culprit vessel). The criteria used for the assignment of the TIMI grade were previously described.[4] Door-to-sheath insertion and door-to-balloon times were defined as the time difference between the arrival of the ambulance service unit at the PCI centre and the sheath or balloon insertion in the catheterisation laboratory.

Data collection for the study was carried out with the written approval of the patients. Data handling and collection was approved by the institutional review boards of the Department of Cardiology, University of Debrecen, Hungary and the Hungarian National Ambulance Service.

Statistical analysis

A statistical analysis was carried out using the GB-Stat v8.0 program. Depending on the type of variable (qualitative or quantitative parameter), the descriptive methods applied involved the calculation of absolute and relative frequencies, or calculation of the mean and standard deviation (SD). Normally distributed continuous variables were compared using Student's t test at an α-level of 5%. Categorical variables (baseline parameters, clinical events and medication) were compared by means of the Wilcoxon rank-sum test at an α-level of 5%.

Variables with significant differences ($p < 0.05$) between groups (hospital death group and control group) were assessed by applying univariate logistic regression model and quantified for odds ratios and 95% confidence intervals (CIs). For multiple regression, cogent predictors of mortality displaying a p value of <0.05 in univariate analysis were selected and analysed. For accurate risk assessment, the number of variables in the multiple regression model was limited. Also, a p value of <0.05 was considered to be significant. For the cumulative survival analysis, the Cox regression model (conditional logistic regression) was applied.

Results

Altogether, 775 STEMI patients were involved in the study (49 patients in the hospital death group and 726 patients in the control group). The total in-hospital mortality on day 20 was 6.32% (49 patients). The frequency of deaths was highest at the beginning of hospitalization (24 deaths occurred on day 1). After day 20 there was no hospital death in this patient's cohort. The cause of death in all cases was infarct-related (cardiogenic shock, asystole, cardiac tamponade, arrhythmias and stent thrombosis).

Baseline characteristics of the hospital death group and those of the control group are listed in Table 1. The two groups were not significantly different regarding risk factors and previous medical history. However, the patients in the hospital death group were slightly, but significantly ($p = 0.0006$) older as compared to controls. Proportionally, significantly ($p = 0.0361$) more TTECG-based consultations were carried out in the control group as compared to the hospital death group (Table 1).

The incidence of pre-hospital AHF and successful resuscitation were – as expected – significantly higher in the hospital death group compared to controls (Table 1). The pre-hospital medical therapy is summarised in Table 2. In the control group, significantly more acetylsalicylic acid (ASA)/clopidogrel, sodium-heparin (5000 U bolus), low-dose nitroglycerin infusion and upstream or downstream glycoprotein (GP) IIb/IIIa inhibitor (eptifibatide) were used by the paramedics or cardiologists. The majority of GP IIb/IIIa inhibitor administration (>90%) was carried out downstream. Nevertheless, in the hospital death group significantly more atropine and intravenous inotropes were administered prior to hospital admission compared to controls.

An examination of the coronary angiograms in patients revealed that the total occlusion rate of the infarct-related artery before PCI was significantly higher in the hospital death group as compared to controls ($p = 0.0462$, Table 2). This finding was in accordance with the lower frequency of pre-hospital

Table 1. Baseline characteristics of patients.

	Hospital death group (n=49)	Control group (n=726)	p value
General			
Age (years)	66.61±12.09	60.63±11.76	0.0006
Men (%)	65.30	67.21	0.7830
Anterior myocardial infarction (%)	53.06	46.20	0.3834
TTECG based consultation (%)	36.73	51.99	0.0361
AHF (Killip >2) (%)	30.61	4.41	<0.0001
Pre-hospital resuscitation (%)	32.65	5.23	<0.0001
Previous history (%)			
Myocardial infarction	16.32	9.22	0.1041
Stroke	6.12	3.72	0.3989
Congestive heart failure	16.32	10.61	0.2152
PCI	10.20	7.71	0.5312
Previous cardiac risk factors (%)			
Hypertension	69.38	67.58	0.7942
Diabetes mellitus	30.61	21.21	0.1232
Hypercholesterolaemia	44.89	55.64	0.1435

AHF: acute heart failure; ECG: electrocardiogram; PCI: percutaneous coronary intervention; SD: standard deviation; TTECG: transtelephonic ECG.

Values are means±SD or percentages of subjects. Here, the p value refers to differences between the hospital death group and the control group.

Table 2. Pre-hospital medical therapy and PCI procedural details of the study population.

	Hospital death group (*n*=49)	Control group (*n*=726)	*p* value
Pre-hospital medical therapy (%)			
Acetylsalicylic acid and/or clopidogrel	65.91	91.41	<0.0001
Sodium heparin	69.38	81.40	0.0394
Nitroglycerin infusion	4.08	24.24	0.0012
Narcotics	44.89	47.10	0.7644
Atropine	20.41	5.92	<0.0001
Beta-blocker	8.1	4.9	0.2513
Intravenous inotropes	20.41	3.85	<0.0001
GP IIb/IIIa inhibitor	22.44	37.19	0.0379
PCI procedural parameters			
Stent/patient (mean±SD)	0.90±0.94	1.35±0.82	0.0002
Drug eluting stent (%)	4.08	4.54	0.8798
LAD[a] (%)	53.06	50.54	0.7832
CX[a] (%)	20.40	19.55	0.8945
RCA[a] (%)	34.67	37.46	0.7930
Total occlusion before PCI (%)	73.33	54.75	0.0462
Intracoronary thrombus before PCI (%)	80.03	64.81	0.0883
TIMI flow before PCI	0.93±1.36	1.16±1.37	0.3049
Door to sheath insertion time (min)	55.85±22.78	44.31±17.20	0.0001
Door to balloon insertion time (min)	70.20±26.01	61.15±18.63	0.0039

CX: left circumflex; LAD: left anterior descending; PCI: percutaneous coronary intervention; RCA: right coronary artery; SD: standard deviation.

The values are means ± SD or percentages of subjects. The *p* value denotes the differences between the hospital death group and the control group.

[a]Patients may have had interventions on more than one vessel.

antithrombotic medication used. Similar to the total occlusion rate, the intracoronary thrombus rate before PCI was slightly higher amongst hospital deaths compared to controls (80.03% *vs.* 64.81%), but the difference was statistically not significant. The door-to-sheath and door-to-balloon insertion times were significantly longer in the hospital death group (Table 2). An examination of the TIMI flow before PCI revealed no significant difference between the two groups (Table 2).

All the predetermined parameters with significant differences ($p < 0.05$) between groups were assessed by the univariate log-rank test (Figure 1), and odds ratios and CIs for in-hospital mortality were calculated. With the univariate statistical method, various basic data, drug therapy specific parameters and PCI procedural findings were found to have a significant influence on the in-hospital mortality of STEMI patients. Our data analysis showed that age, the presence of pre-hospital AHF, successful resuscitation, door-to-sheath insertion time, door-to-balloon inflation time and total occlusion of the infarct-related artery before PCI were associated with significantly increased odds ratios (Figure 1). At the same time, the TTECG-based consultation and an adequate pre-hospital medical therapy (sodium heparin, ASA and/or clopidogrel, GP IIb/IIIa inhibitor and nitrate infusion) significantly lowered the odds ratios of in-hospital mortality (Figure 1).

Baseline characteristics and treatment related variables with a $p < 0.05$ in the univariate analysis were selected for multiple regression and were quantified for odds ratios and CIs for in-hospital mortality. Interestingly, the TTECG-based consultation and triage (odds ratio 0.48, CI 0.25–0.92, $p = 0.0261$) proved to be a significant independent predictor of a lower risk. Regarding pre-hospital medical therapy, the administration of ASA and/or clopidogrel (odds ratio 0.36, CI 0.15–0.89, $p = 0.0271$) and GP IIb/IIIa inhibitor (odds ratio 0.49, CI 0.24–0.99, $p = 0.0476$) were the most important independent predictors of a decreased risk in this model. Despite this, age (odds ratio 2.33, CI 1.58–3.43, $p = 0.0001$), AHF (odds ratio 3.98, CI 1.55–10.22, $p = 0.0041$) and successful pre-hospital resuscitation (odds ratio 5.85, CI 2.28–15.04, $p = 0.0002$) were the most important independent predictors of an increased risk.

All the other parameters in question that were below $p < 0.05$ in the univariate analysis (i.e. sodium heparin, atropine, inotropes and nitrate infusion) were not found to be significant independent predictors of in-hospital mortality.

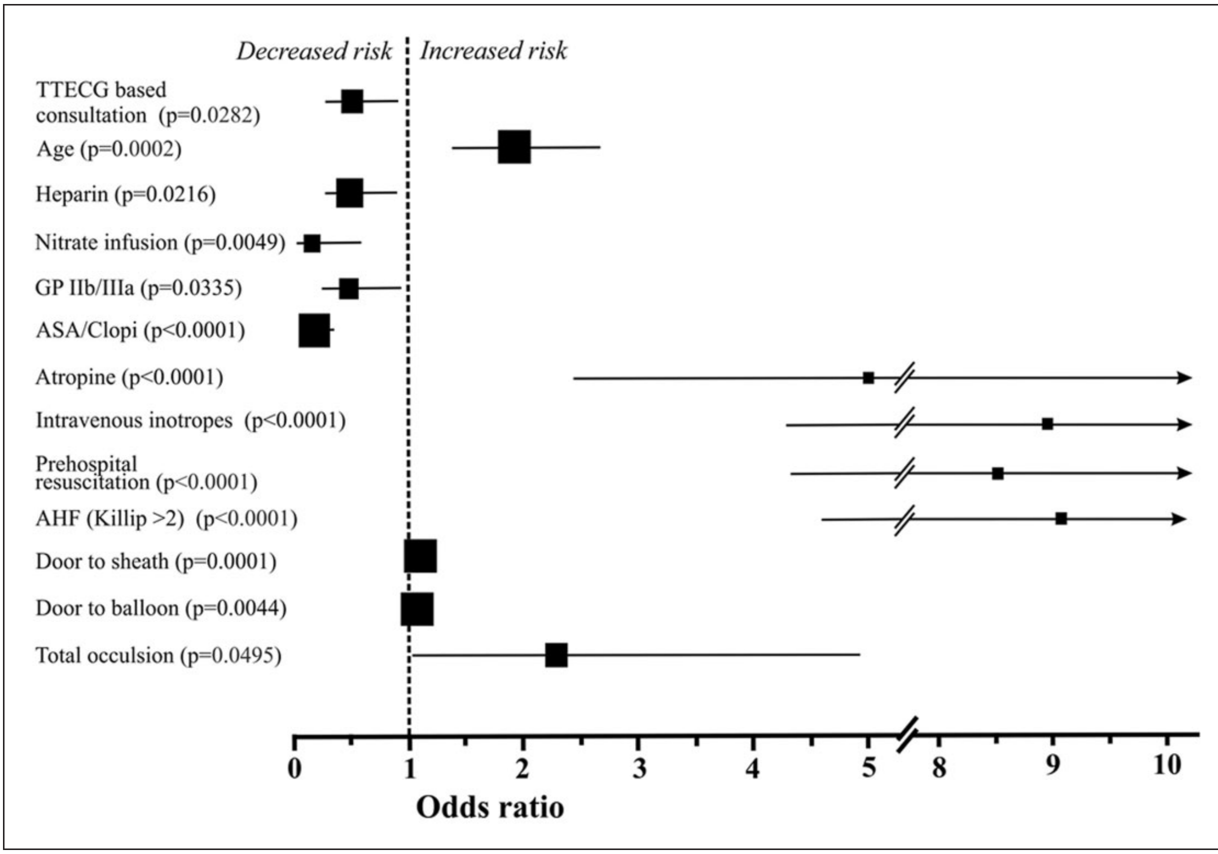

Figure 1. Odds ratios and 95% confidence intervals for hospital mortality in the different subgroups, defined according to baseline characteristics, pre-hospital medical therapy and percutaneous coronary intervention related procedural data. The size of each symbol is proportional to the number of patients in each group. In the case of some parameters (door-to-sheath time and door-to-balloon time and acetylsalicylic acid and/or clopidogrel), the confidence intervals are within the symbols.
AHF: acute heart failure; ASA/clopi: acetylsalicylic acid and/or clopidogrel; Door-to-sheath: door-to-sheath insertion time; Door-to-balloon: door-to-balloon insertion time; GP IIb/IIIa: glycoprotein IIb/IIIa inhibitor; TTECG: transtelephonic electrocardiogram.

Lastly, while examining the PCI procedural data (total occlusion, door-to-sheath and door-to-balloon insertion times), the most important independent predictor of in-hospital mortality was the total occlusion of the infarct-related artery before PCI (odds ratio 5.92, CI 1.03–33.70, $p = 0.0448$).

Discussion

In a previous study we observed that, in a population of STEMI patients, TTECG-based consultation with cardiologists contributed to a significantly lower in-hospital mortality rate.[3] This finding was somewhat unexpected, and it was hypothesised that the benefit of the TTECG-based consultation was due to improved pre-hospital medical therapy and consequently enhanced coronary artery perfusion on hospital admission.[3] Indeed, in the present study we have shown that adequate pre-hospital medical therapy (administration of ASA and/or clopidogrel, GP IIb/IIIa inhibitor and sodium heparin) decreased: (a) the total occlusion rate of the infarct-related artery and (b) the risk of in-hospital mortality. Moreover, our findings strongly suggest that the TTECG and the TTECG-based adequate pre-hospital medical therapy (administration of ASA and/or clopidogrel and GP IIb/IIIa inhibitor) and the total occlusion of the infarct-related artery before PCI are important independent predictors for a lower in-hospital mortality rate.

It is generally accepted that total occlusions and intracoronary thrombi are directly associated with lower coronary flow, myocardial damage and loss of function. Yet, better coronary flow translates into improved myocardial protection and function and ultimately, to an increased survival rate. Based on this assumption, it was demonstrated in the Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention (ASSENT-4 PCI) trial that suboptimal antithrombotic pre-hospital treatment (underuse of sodium-heparin) in STEMI patients might lead to a higher mortality.[5]

In accordance with this finding, our current results indicate that the underuse of pre-hospital sodium heparin, ASA and/or clopidogrel and GP IIb/IIIa inhibitor may have a major impact on coronary patency before PCI. In the recent European Society of Cardiology (ESC) guidelines on STEMI and on myocardial revascularization, great emphasis is placed on early and complete revascularization.[1,6] If primary PCI cannot be performed within 120 min after STEMI diagnosis, fibrinolytic therapy is recommended, provided that there are no contraindications (class IA recommendation).[1] To reduce the time spent before treatment fibrinolysis was proposed even in the pre-hospital setting.[1] Theoretically, the coronary perfusion and prevention of intracoronary thrombi and occlusion are also equally important for STEMI patients undergoing primary PCI. Consequently, the early and adequate pre-hospital antithrombotic therapy prior to primary PCI should be emphasised and supported.[7–9] In the ESC/European Association for Cardio-Thoracic Surgery (EACTS) guideline on myocardial revascularization,[6] the administration of ASA and/or clopidogrel and (upstream) GP IIb/IIIa inhibitor prior to primary PCI are class I and class IIb recommendations, respectively. The downstream use of a GP IIb/IIIa inhibitor ('in-lab' use) for bailout or evidence of a thrombotic complication is a class IIa recommendation.

According to recent guidelines, upon suspected STEMI a 12-lead ECG must be acquired and interpreted as soon as possible at the time of first medical contact in order to facilitate an early diagnosis and triage.[1] For this purpose, the TTECG seems to be an adequate tool. With the TTECG not only can the recording be retrieved and stored, but there is also the immediate possibility for a triage of patients. It has been shown that the early pre-hospital triage with telemedicine in subjects with STEMI undergoing primary PCI significantly reduces the time spent before treatment,[3,10] while improving pre-hospital management.[3,11] Pre-hospital TTECG triage has been shown to associate with higher rates of timely reperfusion both in patients close to the PCI laboratory and even in rural areas.[11]

Moreover, the use of telemedicine in pre-hospital triage of STEMI patients has been shown to be associated with lower mortality rates in both observational studies[3,12,13] and meta-analyses.[10,14] The benefit seems to be even larger in higher risk subjects.[13,15] These remarkable findings on mortality[3,10,12–15] are probably mediated by a reduced time-to-effective treatment (i.e. the reduction of ischaemic time and necrotic area) and better pre-hospital care consequent to pre-hospital triage with telemedicine.[16] In accordance with these observations, the TTECG-based teleconsultation and triage combination in our present study was found to be an independent predictor of lower in-hospital mortality rate.

In the present study, we demonstrated that the successful pre-hospital resuscitation of STEMI patients and AHF (Killip class > 2) are important independent predictors of in-hospital death. These observations are in line with those of previous reports.[17,18] The resuscitation procedure itself explains why a significantly higher amount of atropine and intravenous inotropes in these patients (hospital death group) was used. Moreover, the haemodynamic instability of these patients following resuscitation usually contraindicates the use of nitrates. This explains the lower nitrate use in the hospital death group.

Conclusions

In summary, our findings indicate that a previously published higher in-hospital survival rate of STEMI patients elicited by TTECG-based teleconsultation[3] is associated with better coronary flow in response to improved pre-hospital medical therapy. According to our data: (a) an early, TTECG-facilitated diagnosis of STEMI and a triage of patients, (b) optimal pre-hospital antithrombotic therapy (administration of ASA and/or clopidogrel and GP IIb/IIIa inhibitor) and (c) the patency and better perfusion of the infarct-related artery before PCI are important independent predictors of a lower in-hospital mortality rate (i.e. higher survival rate).

Limitations of the study

The limitation of our study is the fact that all data analyses were carried out on a retrospective basis and on a relatively small sample size (hospital death group; $n = 49$). However, during data collection great efforts were made to standardise the database: the two groups (hospital death and control) were not significantly different regarding risk factors and previous medical history, a relatively long inclusion time (two years) was used in the study and all STEMI patients were included in the database.

Another limitation of our study is that treatment effects were concluded through observational data. There may have been other variables that were not taken into consideration in our model.

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Declaration of Conflicting Interests

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