Original Article

موضوع أصيل

THROMBOLYSIS IN YEMENI PATIENTS WITH ACUTE CORONARY SYNDROME, FACTS AND PROGNOSIS. DATA FROM GULFRACE (GULF REGISTRY OF ACUTE CORONARY EVENTS)– PHASE I

انحلال الخثرة عند المرضى اليمنيين المصابين بالمتلازمة الإكليلية الحادة، الحقائق والإنذار. بيانات سجل الخليج للحوادث الإكليلية الحادة– المرحلة الأولى GULFRACE

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ملخص البحث

هدف البحث: تعتبر الاستعادة السريعة لتروية الشرايين التاجية بعد حدوث المتلازمة الإكليلية الحادة ACS واحتشاء العضلة القلبية مع ارتفاع القطعة ST حجر الزاوية في المعالجة. ونظراً لعدم وجود برنامج للتدخل الأولي للشرايين التاجية عبر الجلد في اليمن فإن استخدام المعالجات الحالة للخثرة هي الوسيلة الأساسية لاستعادة التروية الإكليلية. تهدف هذه الدراسة إلى تسليط الضوء على حجم مشكلة المتلازمة الإكليلية الحادة عند المرضى اليمنيين، عوامل الخطورة المرافقة، معدلات استخدام حالات الخثرة، معدلات المراضة والوفيات لدى هؤلاء المرضى.

طرق البحث: تمثل دراسة Gulf Race دراسة مسحية استباقية متعددة المراكز ومتعددة البلدان للمرضى المقبولين في المشفى بتشخيص نهائي بوجود المتلازمة الإكليلية الحادة في 6 دول عربية في منطقة الخليج والجزيرة العربية خلال مدة 6 أشهر.

النتائج: وجد 1054 من المرضى اليمنيين في دراسة Gulf Race بحالات المتلازمة الإكليلية الحادة، خضع 218 فقط للمعالجة الحالة للخثرة من أصل 750 مريضاً بحالة احتشاء عضلة قلبية مع ارتفاع القطعة ST أو حصار الحزمة الكهربائية اليسرى القلب جديد المنشأ. شكل هؤلاء المرضى نسبة 41% فقط من مجمل الحالات المرشحة لتطبيق المعالجة الحالة للخثرة (531 حالة). بلغ متوسط أعمار المرضى 55.9±11.01 سنة وكان غالبيتهم من الذكور. أورد وجود تدخين عند 127 مريضاً (58.3%)، مضغ القات عند 163 مريضاً (74.3%) بينما سجل وجود فرط في التوتر الشرياني في 57 حالة (26.1%) وداء سكري من النمط الثاني عند 54 مريضاً (24.8%). أورد حدوث قصور القلب الاحتقاني بعد إجراء المعالجة بحالات الخثرة عند مرضى المتلازمة الإكليلية الحادة في 11.5% من الحالات مع حدوث وفيات عند 14 مريضاً (6.4%).

الاستنتاجات: تعتبرنسبة حدوث المتلازمة الإكليلية الحادة في اليمن واحدة من أعلى النسب الملاحظة في المنطقة. إن المعدلات المنخفضة لتطبيق المعالجة بحالات الخثرة كخط أول في المعالجة لإعادة التروية ووصول المريض المتأخر للمشفى تساهم في ضياع فرصة ذهبية لاستعادة التروية التاجية وهو ما يزيد من معدلات المراضة والوفيات. يجب العمل على زيادة برامج التوعية عند المجتمع ولدى الأطباء لتحسين تدبير حالات المتلازمة الإكليلية الحادة.

ABSTRACT

Objective: *Rapid coronary revascularization after ACS with ST elevation acute myocardial infarction (STEMI) is a cornerstone in management. Yemen where no primary Percutaneous Coronary Intervention*

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available, utilizing thrombolytic therapy is the main tool for coronary reperfusion. The major objective was to highlight the magnitude of ACS among Yemeni patients, predisposing risk factors to ACS, the rate of use of thrombolytic therapy, the morbidity and mortality among those patients.

Methods: *Gulf Race I is a prospective, multinational, multicenter survey of patients hospitalized with the final diagnosis of ACS in six Arabian Peninsula/Gulf countries over a period of six month.*

Results: *1054 Yemeni patients with ACS participated in the Gulf Race I, only 218 patients had received thrombolytic therapy out of 750 cases of STEMI or newly developed LBBB. Those 218 patients represent only 41% of all the cases (531 cases) eligible for thrombolytic therapy. The mean age 55.9±11.01 years and were mainly males. Streptokinase was commonly thrombolytic used (95.4%). Smoking reported in 127 patient (58.3%), khat chewing in 163 patient (74.3%) while arterial hypertension in 57 cases (26.1%) and diabetes mellitus type II in 54 patients (24.8%). The mean door to needle in those patient was 59.1 minutes. Heart failure in ACS group after thrombolytic therapy was reported in 11.5% of the patients and death in 14 patients 6.4%.*

Conclusions: *ACS among Yemeni is one of the highest in the area, in spite of low rate of using thrombolytic therapy as a first line of revascularization in Yemen, still the time of presentation of the patient with ACS to the hospitals is late. Missing the golden hours for thrombolytic therapy in Yemeni patients with ACS is associated with high rate of morbidity and mortality. Community and physician awareness programs are needed for better management of ACS.*

INTRODUCTION

The instant reestablishment of coronary blood flow is the major goal in the treatment of (STEMI). Myocardial reperfusion in STEMI is essential to myocardial salvage and improved outcomes.[1] Reperfusion with restoration of antegrade epicardial flow with either thrombolysis or primary percutaneous coronary intervention (PCI) reduces mortality in (STEMI).[2]

A meta-analysis comprising 23 studies, indicates that primary PCI is superior to thrombolysis in reducing death nonfatal reinfarction, and stroke at short -and long-term follow-ups. The result has led to the recommendation of primary PCI as the first-choice reperfusion therapy.[2] Countries with no facilities to establish a primary PCI programs, thrombolytic therapy remains the reperfusion method of choice. The benefits of thrombolytic therapy in patients with AMI are well established in the meta-analyses by Yusuf et al[3], and by the Fibrinolytic Therapy Trial lists (FTT) Collaborative Group who showed that thrombolytic therapy decreases mortality at 35 days by 1.9%.[4]

Yemen is one of the countries participated in (Gulf Race -I), a limited resources country with no program of primary PCI yet, exposure of the Gulf Race I data regarding Yemeni patient with ACS aiming to highlight the magnitude of ACS among Yemeni patients.

METHODS

Gulf Race is a prospective, multinational, multicenter survey of consecutive patients hospitalized with the final diagnosis of ACS in six Arabian Peninsula/Gulf countries over a period of six months. An attempt was made to include everyone with the final diagnosis of ACS, and there were no exclusion criteria. The study received ethical approval from the institutional ethical bodies in all participating countries. Over a six month period which represents phase I Gulf Race. This registry is a descriptive study of 65 medical centers who confirmed their participation and enrolled patients according to the survey inclusion criteria. Over all participants' numbers from all Gulf States were 8176 patients out of them there were 1054 Yemeni patients with ACS pointing out the cases of ST Elevation Acute Myocardial Infarction (STEMI) or newly developed Left Bundle Branch Block (LBBB) who are eligible for thrombolytic therapy.

Diagnosis of the different types of ACS and definitions of data variables were based on the American College of Cardiology (ACC) clinical data standards, published in December 2001.[5-7] These definitions are based on clinical presentations, electrocardiogram

(ECG) findings and cardiac biomarkers. Data collected included patients' demographics, past medical history, provisional diagnosis on admission and final discharge diagnosis, clinical features at hospital presentation, ECG findings, laboratory investigations, early in-hospital (administered within 24 hours of admission) and discharge medications, use of cardiac procedures and interventions, in-hospital outcomes and in-hospital mortality. All management decisions were at the discretion of the treating physician.[8] Data collected were subjected to statistical analysis Continuous variables are summarized as median and inter-quartile ranges and compared using the Wilcoxon rank sum test. Categorical variables are summarized as percentages and compared using χ^2 tests. Step-wise, multivariable logistic regression was used to identify independent predictors of in-hospital morbidity and mortality, the estimated odds ratio (OR) against age as a continuous variable. All associations from the logistic regression models are quantified as OR with 95% confidence intervals. Analyses were performed with SPSS version 20 statistical package (IBM Corporation 1 New Orchard Road Armonk, NewYork10504-1722 United States).

RESULTS

Out of 1054 Yemeni patients with ACS participated in the Gulf Race Phase I over a six month period, only 218 patients had received thrombolytic therapy out of 750 cases of STEMI or newly developed LBBB. Those 218 patients represent only 28% on all cases of STEMI or new LBBB eligible for thrombolytic therapy 264 patients (patients presented 12 hours or less from the start of symptoms). Out of those 10 were subjected to ad-hoc primary PCI by visiting teams. 218 patients received thrombolytic therapy, 36 patients did not receive any reperfusion therapy (13.6%) of all eligible cases of thrombolytic therapy, this percentage represent the shortfall of reperfusion therapy, Figure 1. The mean age was 55.97±11.01 years, with a male predominance (82.6%) in contrast with female patients, Table 1.

Streptokinase was the most commonly used preparation among the thrombolytic drugs (95.4%) followed by Reteplase (4.1%) and t-PA (0.5%) respectively, Table 2. The clinical presentation shows prominent smoking habit in 127 patient (58.3%), khat chewing in 163 patient (74.3%) while arterial hypertension was documented in 57 cases (26.1%), diabetes mellitus type II in 54 patients (24.8%), hyperlipidemia mia in 22 patients (10.1%) and family history of IHD was recorded in 34 cases (17%).

Patient baseline characteristics	STEMI patients with thrombolytic therapy
No. (%)	218 (28%)
Age (Mean±SD) years	55.97±11.01
Male gender	180 (82.6%)
Diabetes mellitus	54 (24.8%)
Hypertension	57 (26.1%)
Hyperlipidemia	22 (10.1%)
Smoking habits	127 (57.3%)
Khat chewing	163 (74.3%)
Family history of IHD	34 (17%)
Prior PCI	7 (3.2%)
Old MI	19 (8.7%)
Prior CABG	3 (1.7%)

AMI=acute myocardial infarction, CABG=coronary artery bypass grafting, IHD=ischemic heart disease.
PCI=percutaneous coronary intervention.

Table 1. Baseline clinical characteristics of STEMI patients who received thrombolytic therapy.

Patients with history of previous MI was recorded in 19 patients (8.7%) while 7 patients had PCI prior to episodes of ACS and only three (1.7%) had CABG in the past. Location of ST segment elevation in ECG was predominantly in inferior leads (29.8%) followed by extensive anterior leads (24.3%) and anterioseptal leads (18.3%), Table 2. The mean door to needle in those patient was 59.1 minutes (±102.6 SD).

Congestive heart failure was the most common sequel in ACS group after thrombolytic therapy (11.5%), while cardiogenic shock was documented in 9.2%, tachyarrhythmia were noted in 6% and major bleeding in one patient (0.5%). Mortality in 14 patients 6.4%.

DISCUSSION

Whereas the medical and technological improvement in the last 3 decades has enhanced clinical outcomes in

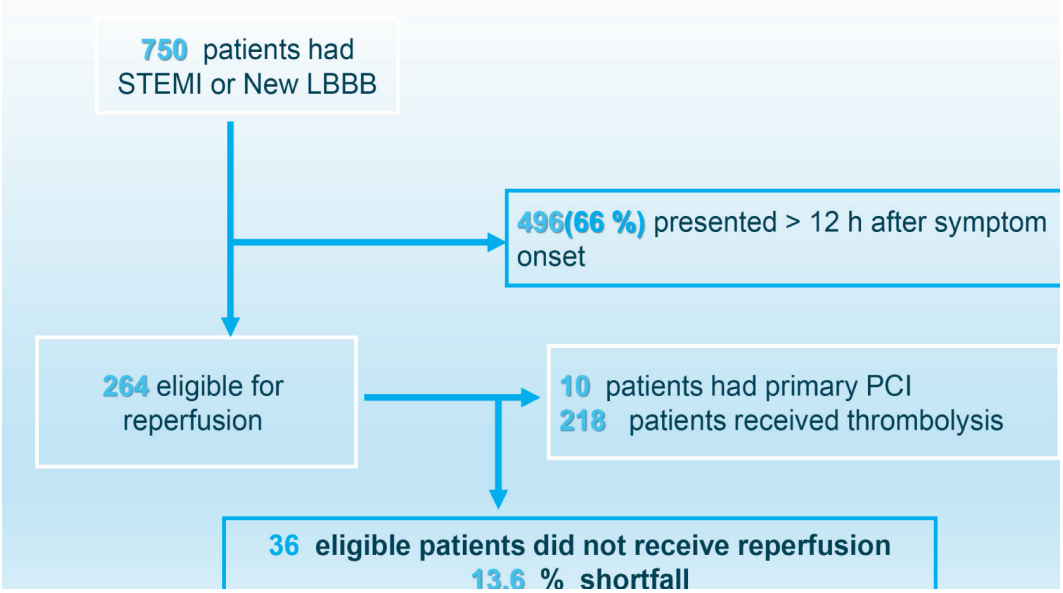

Figure 1. Thrombolytic therapy and missed opportunity for reperfusion.

Site of AMI	Frequency	%
Anterior+inferior	7	3.2
Antero-lateral	19	8.7
Antero-septal	40	18.3
Extensive anterior	53	24.3
High lateral	2	1
Inferior	65	29.8
Inferior+RV	9	4.1
Infero lateral	12	5.5
Inferior-posterior	9	4.1
Lateral	2	0.9

Table 2. Location of AMI in patients received thrombolytic therapy.

Thrombolytic agent	Frequency	%
Streptokinase	208	95.4
Tissue Plasminogen Activator (tPA)	1	0.5
Reteplase	9	4.1

Table 3. Type of thrombolytic agent used.

patients presenting with acute STEMI, residual morbidity and mortality are still high. Randomized controlled trials of thrombolytic therapy have demonstrated the benefit of initiating treatment as early as possible after the onset of STEMI symptoms.[9,10] This is the first data from Yemen regarding reperfusion after ACS over 6 month period, Yemen represents a low income country in middle east.[11] Data from GulfRace I indicates that nearly one-third of patients with STEMI in the Arabian Gulf presented to the hospital 12 hours after symptom onset. Morbidity and mortality related to this delay in coronary reperfusion among those patients.[12]

Yemen data analysis is consistent with data of the Gulf-Race phase I[13] as well as previous reports from other registries. The delayed presentation rate (>12 hours) 8.7%[14,15] was reported in a supplementary study of the National Registry of Myocardial Infarction (NRMI). The GRACE registry indicated that only 70.5% of the cases had presented within 12 hours of symptom onset.[16]

Cohen et al reported that 40% of acute STEMI patients presented >12 hours after symptoms onset, female gender and older age were independent predictors of late presentation.[17] Yemen data shows the highest rate of late presentation, nearly 66% of patients presented late. This could be related to the socioeconomic status and literacy rate (65.3%)[18] may play an important role in late presentation. Advocacy programs directed toward medical and patient population may have impact the early presentation

rate. The high reperfusion shortfall rate in Yemen data 13.6% may reflect the lack of organization of health facility, the lack of national treatment protocols and scarcity of training of medical teams. Many limitations were noted in our study. Although our cohort included nearly consecutive patients with suspected ACS, only 85% of the cases were included. Nearly 60% of the study cohort had ejection fraction assessment, and only a minority of patients underwent coronary angiography. The socioeconomic status of patients and their literacy rate were not included. In addition, there were no information about the credentials of treating physicians and the impact of specialized training on shortfall rate.

CONCLUSIONS

GulfRace I is an awakening call for practicing cardiologists and health care providers in the Gulf.

Exposure of practice: doing well with certain aspects of care, but doing poorly with other aspects.

There is a large gap between what is known and what is done in daily practice. Cardiologists in the area needed to get together to breach this gap. Prevalence of ACS among Yemeni patients is one of the highest in the area in spite of low rate of using thrombolytic therapy as a first line of revascularization in Yemen. Still the time of presentation of the patient with ACS to the hospitalsis late. Missing the golden hours for thrombolytic therapy in Yemeni patients with ACS is associated with high rate of morbidity and mortality. Community and physician awareness programs are needed to increase the utilization of better management of ACS.

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