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Quantitative myocardial blush score (QuBE) allows the prediction of heart failure development in long-term follow-up in patients with ST-segment elevation myocardial infarction: Proof of concept study

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Abstract

Background: *Acute myocardial infarction (AMI) might lead to left ventricular remodeling. Adequate myocardial perfusion is critical to prevent this adverse remodeling. Quantitative myocardial blush evaluator (QuBE) software, available on-line, is a simple analysis tool which enables the precise quantification of myocardial perfusion in the infarct area immediately after interventional treatment. The aim of this study was to assess whether the results of QuBE analysis might predict the development of heart failure (HF) in AMI patients in 3 year-long follow-up.*

Methods: *Ninety five patients with first AMI, single vessel coronary artery disease, Killip class I at presentation were enrolled in the study. Angiograms were reanalyzed using the on-line QuBE software. Data on heart failure development (ICD 10 codes I50) provided by the National Health Fund were considered as primary outcome.*

Results: *QuBE values ranged from 0.0 to 25.3 arbitrary units, mean value was 9.9 ± 5.2 arbitrary units. QuBE correlated positively with myocardial blush grade (MBG; Spearman $R = 0.342$ at $p < 0.05$). Multivariate Cox proportional hazard modeling, adjusted for initial Thrombolysis in Myocardial Infarction (TIMI flow, and TIMI thrombus grade indicated QuBE score (1 unit increase — HR 0.919, 95% CI 0.846–0.999, $p = 0.049$) and left ventricular ejection fraction at discharge (1% increase — HR 0.936, 95% CI 0.902–0.971, $p = 0.000$) as independent predictors of HF development.*

Conclusions: *The QuBE assessment of myocardial perfusion allows the prediction of HF development in the post-infarction period in this highly selective group of patients.* (Cardiol J 2019; 26, 4: 322–332)

Key words: acute myocardial infarction, left ventricular remodeling, primary percutaneous coronary intervention, quantitative myocardial blush evaluator

Introduction

The advent of interventional treatments for acute myocardial infarction (AMI) has greatly improved patient survival. Despite continuous progress in interventional tools and techniques, immediate results of primary coronary angioplasty remain far from optimal. Up to 40% of patients with restored normal epicardial blood flow Thrombolysis in Myocardial Infarction (TIMI) III has impaired myocardial perfusion [1] and microvascular obstruction arises as a major obstacle in complete heart muscle recovery [2, 3]. Coronary microvascular dysfunction is responsible for infarct expan-

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sion and adverse remodeling of the left ventricle (LV) [4] and might eventually result in overt heart failure (HF) [5].

Myocardial blush grade (MBG), an angiographic measure of myocardial perfusion, was proven to correlate with enzymatic infarct size, echocardiographically assessed left ventricular ejection fraction (LVEF) [6], mortality [6, 7], and higher incidence of LV remodeling [1]. Moreover, authors of the latter paper [1], have reported almost 60% incidence of signs and symptoms of congestive HF within 6 months after AMI in patients in whom myocardial perfusion was inadequate (MBG 0 and 1) after primary coronary angioplasty. There are also contradictory data and several small studies have reported the lack of correlation between MBG and myocardial perfusion assessed by contrast echocardiography [8, 9]. Furthermore, Bertomeu-Gonzalez et al. [10] have raised the question on inter-observer variability of MBG assessment, have reported on a lack of correlation between MBG and LVEF assessed with magnetic resonance imaging (MRI). Authors of additional studies point out superior performance of TIMI myocardial perfusion scale (TMP) over MBG in correlation with other indices of myocardial perfusion [1, 11].

Reference diagnostic methods of perfusion assessment, such as the evaluation of the coronary blood flow velocity [12, 13], myocardial contrast echocardiography [14, 15], or MRI [16, 17], are not widely used for prognostic purposes in post-infarction patients.

A simple, robust, free of operator bias method of myocardial perfusion assessment with an ability to stratify patient risk would be invaluable in clinical practice. The quantitative myocardial blush evaluator (QuBE) software appears to be encouraging in this regard [18]. The QuBE was designed to facilitate an operator-independent assessment of myocardial perfusion. It correlates with other measures of infarct size and myocardial perfusion [18, 19]. Higher QuBE values indicate at improved survival [18] and better LV performance [20].

The aim of this proof-of-concept study was to assess whether the results of a QuBE analysis might be useful to predict HF development in stable, post-infarction patients who had survived their first myocardial infarction (MI).

Methods

Study population

This study is a retrospective review of medical records of patients admitted with ST-segment elevation myocardial infarction (STEMI) between January 2004 and December 2014. Diagnosis of STEMI was based on chest pain lasting more than 20 min, ST-segment elevation in electrocardiography, or positive findings for myocardial necrosis markers. Out of 1469 consecutive patients, 696 patients had incomplete medical records, different myocardial necrotic markers, faded or unreadable electrocardiogram (ECG) tracings, 543 had poor quality of angiograms with short contrast injections and recordings, or with overlapping distal parts of vessels. Out of 230 patients with complete medical data, 95 patients have met inclusion criteria into this single center study (first MI, no evidence of HF at admission or prior to admission, single vessel disease, and major coronary artery LAD, Cx, RCA as infarct-related vessel) and were selected for further analysis with 36 month-long follow-up (Fig. 1). All patients had been treated with primary percutaneous angioplasty. The administration of glycoprotein (GP) IIb/IIIa inhibitors as well as the use of aspiration catheters was at the operator's discretion. Demographic, clinical, procedural, and laboratory data were recorded.

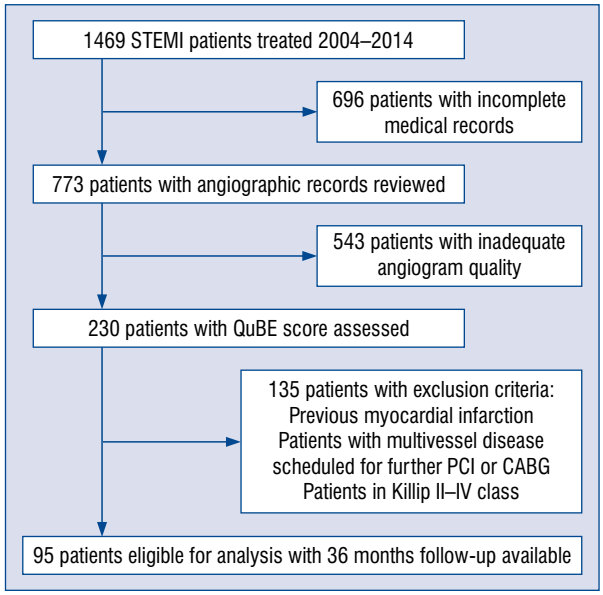

Figure 1. Flow chart of patients with ST-segment elevation myocardial infarction (STEMI) treated from 2004 to 2014; CABG — coronary artery bypass grafting; PCI — percutaneous coronary intervention.

Angiographic assessment

Archived angiographic DICOM records were reanalyzed by a single reviewer (AT). For inter-observer analyses another observer (MO) was

asked to review randomly selected angiograms. Both reviewers were blinded to QuBE score results. The original operator descriptions of the primary percutaneous procedures, which were lacking initial or final TIMI flow values and MBGs, were recorded by the reviewer. For thrombus classification a score proposed by Gibson et al. [21] was used. In patients presenting with an occluded infarct-related artery (IRA) (grade 5 thrombus, essentially no flow), thrombus was reclassified into one of the other categories after flow achievement with either guide-wire crossing or a small (diameter 1.5 mm) deflated balloon passage or dilation [22]. A corrected TIMI frame count was calculated for the IRA in the final angiogram according to Gibson et al. [23]. MBG was evaluated according to van't Hof et al. [6] and was judged in the final angiogram. For the operator-independent evaluation of myocardial perfusion, an on-line software was used. (Quantitative Blush Evaluator available at http://www.stellarjackpot.com/qube/ recently [18]). For detailed intra- and inter-observer variability assessment of myocardial perfusion see **Supplementary material on-line**.

Non-invasive reperfusion, infarct-size, and LVEF assessment

For a non-invasive assessment of myocardial perfusion, the electrocardiographic indices of ST reduction according to van't Hof et al. [24] was used. Electrocardiograms were reviewed by TM, EN, KP, and AI. For assessment of infarct size, peak activity of creatine kinase and troponin T concentration area under the curve (AUC) measured at admission was utilized at 12, 24, and 72 hours. AUC was calculated with formula: TpAUC = 0.5 × Tp0 + 0.5 × Abs(Tp12 – Tp0) + 0.5 × Tp12 + 0.5 × Abs(Tp24 – Tp12) + 2 × Tp72 + Abs(Tp72 – Tp24), where Tp0, Tp12, Tp24, Tp72 are respective troponin concentrations, and Abs is the absolute value of the subtraction. AUC was expressed in ng/L × 24 h (**Suppl. material on-line**). The pre-discharge LVEF, LV end-diastolic volume (LVEDV), and LV end-systolic volume (LVESV) from patients' archives. LVEF was measured using biplane Simpson's method [25] with software integrated in GE Vivid 7 Dimension echocardiography machine (GE Vingmed, Horten, Norway) was recorded. LVEDV and LVESV were indexed for body surface area (BSA) and expressed as mL/m^2. BSA from patient's baseline height and weight according to Mosteller's formula [26] was calculated.

Study endpoint

Study endpoint was the development of new onset HF. International Classification of Diseases, 10th revision (ICD-10) codes I50.0–I50.9 reported to National Health Fund (NHF) were considered as HF development. The present methodological approach followed these steps. First the Silesian Division of NHF was asked to provide us with vital status of patients with respective dates of deaths and the dates when patients were registered with I50.0–50.9 coding numbers. The electronic data file from NHF included multiple entries for some patients with different dates of HF reported to NHF. Additional information was provided by the NHF; the general identifier of medical institution reporting on the patient (internal medicine ward, cardiology ward). The assumption was that the earliest date was the date of new onset HF. One more assumption was accepted: patients with coinciding dates of HF and death were censored in Kaplan-Meier analysis. Then assumptions were validated and cross-checked with source documentation for any annotation of symptoms, signs, and inotropic or diuretic drugs administered which included final diagnosis of new onset HF, and the returned information from NHF on the diagnosis of HF in the observed patients. Eight events of new onset HF were recorded during index hospitalization for STEMI treatment and 8 patients were reported from NHF with the ICD-10 50.0–50.9 numbers. Thus, 8 out 39 cases (approx. 20%) were validated. The date of HF occurrence was assigned as the admission date. An exception was made for patients who had revealed HF symptoms and required administration of diuretics, or inotropic support during the index hospitalization for AMI treatment. The date of symptom appearance and/or administration of drugs, recorded from medical archives was considered as the date of HF development.

Statistical analysis

Quantitative data are presented as the means and standard deviations (or standard error of the mean in cases of necrotic markers) and categorical data are presented as numbers and percentages. Data were analyzed for normal distribution with the Kolmogorow-Smirnov test and for homogeneity of variances with Levene's test. Groups were compared with a Student t test or χ^2 test with Yates correction. Non-parametric correlation as well as linear regression analysis was used to assess relationship of QuBE score with other variables.

Table 1. Demographic and baseline presentation of patients divided into groups according to heart failure (HF) development.

	No HF (n = 56)	HF (n = 39)	Statistics	Significance
Men/women	41/15	23/16	χ^2	NS
Age [years]	61.5 ± 11.4	65.3 ± 12.3	Student's t test	NS
Hypertension	39 (69.6%)	29 (74.4%)	χ^2	NS
Diabetes	17 (30.4%)	13 (33.3%)	χ^2	NS
Hyperlipidemia	29 (51.8%)	21 (53.8%)	χ^2	NS
Smoking	28 (50.0%)	21 (53.8%)	χ^2	NS
Family history	13 (23.1%)	12 (30.8%)	χ^2	NS
Creatinine [μmol/L]	84.2 ± 32.4	85.4 ± 31.8	Student's t test	NS
Body mass index [kg/m^2]	28.0 ± 4.3	28.5 ± 4.3	Student's t test	NS
Body surface area [m^2]	2.0 ± 0.2	1.9 ± 0.2	Student's t test	NS
Infarct location:				
Anterior	22 (39.3%)	19 (48.7%)	χ^2	NS
Inferior	34 (60.7%)	20 (51.3%)		
Symptom duration [min]	387.0 ± 411.0	387.2 ± 278.4	Student's t test	NS
Time door-to-needle [min]	32.5 ± 29.6	33.9 ± 32.4	Student's t test	NS

Receiver operator characteristic (ROC) curves were calculated for HF development and QuBE score as de-stimulating factor. Different discrimination methods for ROC analysis were used. A tangent method provided QuBE score cut-off value of 7.6 arbitrary units with specificity 0.49 and sensitivity 0.68. The Youden method provided a QuBE score cut-off value of 13.3 arbitrary units with specificity 0.9 and sensitivity 0.32. Both cut-off values, as well as QuBE score tertiles were used for Kaplan-Meier survival modeling. HF development in the follow-up was considered as complete observation, any death occurring before HF development was considered as a censored observation. Univariate and multivariate Cox proportional hazard modeling was used to find predictors of HF development. Differences in the means or frequencies were considered significant when $p < 0.05$. Statistica 12 (Statsoft Inc., Tulsa, USA), equipped with the Medical Package (Statsoft Polska, Krakow, PL) was used for data analysis.

Results

QuBE assessment

QuBE values ranged from 0.0 to 25.3 arbitrary units, mean value was 9.9 ± 5.2 arbitrary units. QuBE positively correlates with MBG (Spearman $R = 0.342$ at $p < 0.05$). Reproducibility, variability, and agreement analyses for visual (MBG) and computer-assisted myocardial (QuBE) perfusion assessment indicate increasing diagnostic accuracy of the latter method. Moreover, QuBE scores correlate negatively with symptom duration ($p < 0.05$) (**Suppl. material on-line**).

Clinical and angiographic presentation, procedural outcomes

For clarity of presentation, patients were classified and shown in tables according to clinical status at follow-up: 56 patients without new onset HF (no HF) and 39 patients with new onset HF in the follow-up (HF). Patient demographics and myocardial infarction characteristics are shown in Table 1. Angiographic and procedural data are presented in Table 2. Table 3 presents electrocardiographic assessment of reperfusion, enzymatic infarct size, LV function and volumes at discharge. While the groups are comparable in regard to baseline presentation, they differ significantly in TIMI thrombus classification, QuBE score, troponin concentration, and pre-discharge LVEF. HF group had significantly higher thrombus burden after reclassification — 19 (48.7%) patients had thrombus grade III–V as opposed to 15 (26.8%) patients with thrombus grade III–IV (none with grade V thrombus) in no HF group. This feature was accompanied by lower myocardial perfusion as assessed with QuBE score, higher enzymatic infarct size, and lower LVEF at discharge in HF group.

Table 2. Angiographic and procedural data for groups according to heart failure (HF) development.

	No HF (n = 56)	HF (n = 39)	Statistics	Significance
Infarct related artery:			χ^2	NS
LAD	22 (39.3%)	19 (48.7%)		
Cx	6 (10.7%)	3 (7.7%)		
RCA	28 (50.0%)	17 (43.6%)		
Initial TIMI flow:			χ^2	NS
0	25 (44.6%)	18 (46.2%)		
I	2 (3.6%)	6 (15.4%)		
II	7 (12.5%)	4 (10.2%)		
III	22 (39.3%)	11 (28.2%)		
TIMI thrombus grade initial/reclassified:			χ^2	p = 0.02
0	11/18 (19.6/32.2%)	3/4 (7.7/10.3%)		
I	9/12 (16.0/21.5%)	9/11 (23.1/28.2%)		
II	6/11 (10.7/19.6%)	3/4 (7.7/10.3%)		
III	3/6 (5.4/10.7%)	2/5 (5.1/12.8%)		
IV	1/9 (1.8/16.0%)	2/11 (5.1/28.2%)		
V	26/0 (46.5/0.0%)	20/4 (51.3/10.3%)		
Thrombus aspiration	17 (30.4%)	11 (28.2%)	χ^2	NS
Glycoprotein IIb/IIIa inhibitors:			χ^2	NS
None	27 (48.2%)	20 (51.3%)		
Abciximab	17 (30.4%)	16 (41.0%)		
Integriline	12 (21.4%)	3 (7.7%)		
Stent implantation:			χ^2	NS
BMS	29 (51.8%)	24 (61.5%)		
DES	21 (37.5%)	9 (23.1%)		
Temporary pacing	2 (3.6%)	0 (0.0%)	χ^2	NS
Final TIMI flow:			χ^2	NS
0	1 (1.8%)	3 (7.7%)		
I	2 (3.6%)	3 (7.7%)		
II	3 (5.4%)	4 (10.3%)		
III	50 (89.2%)	29 (74.3%)		
cTFC [Frame/s]	28.6 ± 21.2	37.4 ± 28.9	Student's t test	NS
Myocardial blush grade:			χ^2	NS
0	3 (5.4%)	5 (12.8%)		
I	4 (7.1%)	5 (12.8%)		
II	16 (28.6%)	9 (23.1%)		
III	33 (58.9%)	20 (51.3%)		
AVDE	7 (12.5%)	6 (15.4%)	χ^2	NS
Procedural success	40 (71.4%)	26 (66.7%)	χ^2	NS

AVDE — angiographically visible distal embolization, BMS — bare metal stent; cTFC — corrected TIMI frame count; DES — drug eluting stent; LAD — left anterior descending artery; Cx – circumflex artery; QuBE – quantitative blush evaluator; RCA — right coronary artery; TIMI — Thrombolysis in Myocardial Infarction

Long-term outcome assessment

Follow-up was terminated at 36 months. Events which occurred in the first 36 months were included in the analysis. Patients were followed for a median time of 428 days (interquartile range 60–977 days, mean 528 ± 437.4 days). Patients at discharge from hospital were administered comparable medical treatment (Table 4). According to NHF data, during the follow-up 39 (41.1%) patients were reported to have developed HF.

Table 3. Electrocardiographic assessment of reperfusion, enzymatic infarct size and left ventricle function at discharge in patients divided into groups according to heart failure (HF) development.

	No HF (n = 56)	HF (n = 39)	Statistics	Significance
QuBE [arb. units]	10.8 ± 5.7	8.6 ± 4.1	Student's t test	0.045
ST-segment elevation resolution:			χ^2	NS
None	11 (19.6%)	13 (33.3%)		
Partial	32 (57.2%)	15 (38.4%)		
Complete	13 (23.2%)	11 (28.3%)		
Peak CK-MB [IU/L]	194.2 ± 39.6	237.8 ± 32.1	Student's t test	NS
Troponin T [ng/L]:			Student's t test	NS
Baseline	505.1 ± 92.3	842.3 ± 270.1		
12 h	2751.9 ± 318.2	3590.2 ± 471.7		NS
24 h	2205.8 ± 232.5	3158.2 ± 357.4		0.022
72 h	1472.7 ± 140.9	2069.3 ± 221.9		0.019
TpT AUC [ng/L*days]	6894.7 ± 713.7	9595.8 ± 1034.8		0.029
LVEF [%]	44.0 ± 9.8	38.7 ± 11.6	Student's t test	0.017
LVEDVI [mL/m^2]	62.8 ± 13.6	60.2 ± 16.0	Student's t test	NS
LVESVI [mL/m^2]	34.5 ± 6.8	35.7 ± 7.0	Student's t test	NS

CK-MB — creatine kinase muscle-brain isoenzyme; QuBE — quantitative myocardial blush evaluator; LVEF — left ventricular ejection fraction; LVEDVI — left ventricular end-diastolic volume index; LVESVI — left ventricular end-systolic volume index; TpT AUC — troponin T area under the curve

Table 4. Medical treatment of patients at discharge depending on heart failure (HF) development in follow-up.

	No HF (n = 56)	HF (n = 39)	Statistics	P
Clopidogrel	56 (100.0%)	39 (100.0%)	χ^2	NS
Beta-blockers	54 (96.4%)	38 (97.4%)	χ^2	NS
ACEI/ARB	56 (100.0%)	39 (100.0%)	χ^2	NS
Calcium channel antagonists	9 (16.1%)	4 (10.3%)	χ^2	NS
Statin	54 (96.4%)	36 (92.3%)	χ^2	NS
Oral anticoagulation	9 (16.1%)	7 (17.9%)	χ^2	NS
Loop diuretics	10 (17.9%)	17 (43.6%)	χ^2	NS
Spironolactone	3 (5.4%)	4 (10.3%)	χ^2	NS
Digoxine	1 (1.8%)	1 (2.6%)	χ^2	NS

ACEI — angiotensin converting enzyme inhibitor; ARB — angiotensin receptor blocker

Using two different discrimination methods for ROC analysis two different QuBE score cut-off values were received (Fig. 2). A tangent method provided QuBE score cut-off value of 7.6 arbitrary units with specificity 0.49 and sensitivity 0.68. A Youden's method provided QuBE score cut-off value of 13.3 arbitrary units with specificity 0.9 and sensitivity of 0.32. Both methods yield the same AUC 0.599 at p = 0.08. Both cut-off values, as well as QuBE score tertiles were used for Kaplan-Meier survival modeling and its results are shown in Figure 3 with three different panels for different cut-off values. The QuBE score cut-off value of 13.3 arbitrary units provides the most significant (p = 0.01) difference between the groups in survival without HF development. Univariate Cox proportional hazard analysis has disclosed several demographic, clinical, angiographic, and procedural variables as those related significantly to HF development (Table 5). Of those, initial TIMI flow and thrombus burden after reclassification as primary variables (i.e. variables that existed before or at the very beginning of

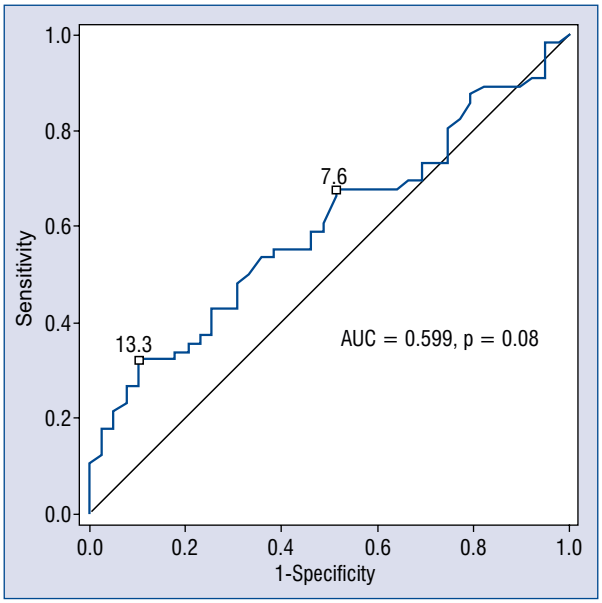

Figure 2. Receiver operator characteristic curve for quantitative myocardial blush evaluator (QuBE) values and heart failure development in 36-month-long follow-up with two different discrimination methods: tangent (QuBE score = 7.6 arb. units) and Youden's method (QuBE score = 13.3 arb. units); AUC — area under the curve.

invasive procedure) were used for stratification of multivariate model. Multivariate model corrected TIMI frame count, QuBE score, troponin T AUC, and the pre-discharge LVEF were introduced, while only QuBE score and LVEF remained independent predictors of HF development in the 36 month-long follow-up (Table 5). During hospital stay 5 patients died: 2 patients within 24 h after primary angioplasty, and 3 more patients died after they have developed HF as the direct causes of all death ventricular arrhythmias. In the follow-up 7 more deaths occurred. They did not coincide with a new onset HF.

Discussion

This study shows results from a quantitative myocardial blush evaluation assessed immediately after interventional treatment of STEMI allowing for prediction of HF development in long term follow-up. Nonetheless it should be underlined that there are some peculiar features of the study population. Enrolled into this study was highly selective population with first time MI, who had been classified in Killip class I. Considering larger

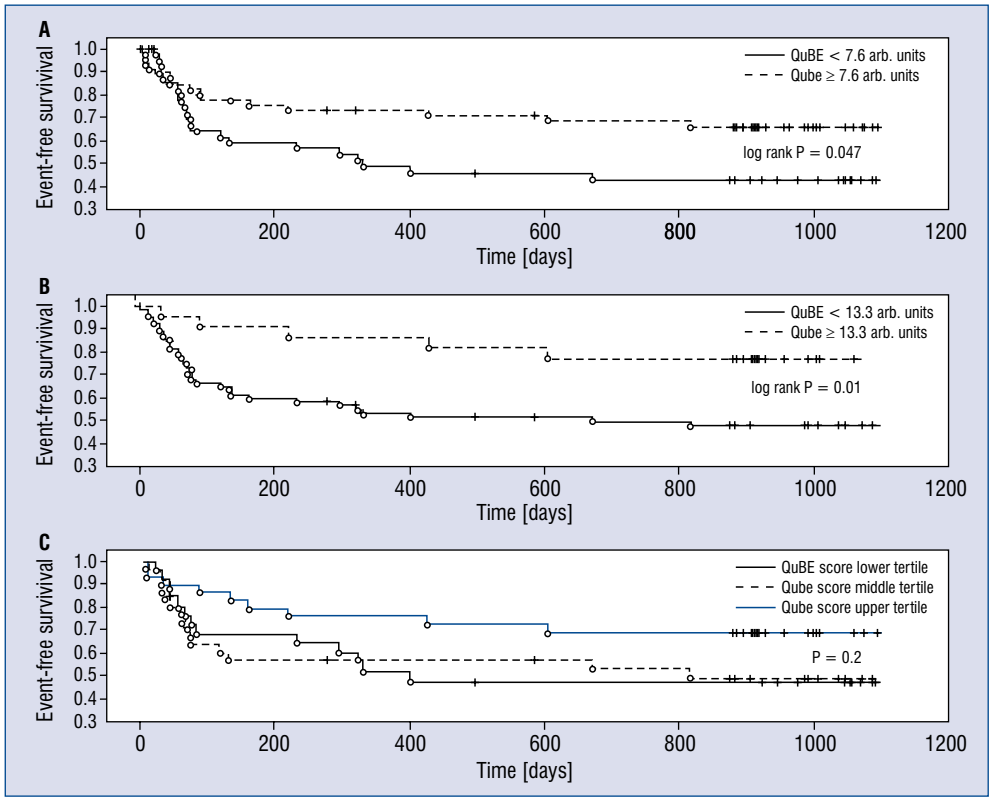

Figure 3. Kaplan-Meier survival curves without heart failure development depending on quantitative myocardial blush evaluator (QuBE) score cut-off value 7.6 arbitrary units (**A**), 13.3 arbitrary units (**B**), and QuBE score tertiles (**C**); °Complete; +Censored.

Table 5. Univariate and multivariate predictors of heart failure development in ST-segment elevation myocardial infarction patients in 36 months-long follow-up.

	Univariate			Multivariate		
	HR	95% CI	P	HR	95% CI	P
Demographic and clinical						
Age (1 year increase)	1.022	0.993–1.051	0.137			
Male sex	0.581	0.301–1.121	0.106			
Body mass index (1 kg/m^2 increase)	1.039	0.961–1.123	0.333			
Diabetes	1.189	0.587–2.404	0.631			
Hypertension	1.087	0.526–2.247	0.821			
Creatinine (1 μmol/L increase)	0.998	0.984–1.012	0.796			
Peak CK-MB activity (1 unit increase)	1.001	1.000–1.003	0.145			
Troponin AUC (1000 ng/L*24 h increase)	1.059	1.010–1.108	0.018	1.015	0.999–1.079	0.634
LVEF (1% increase)	0.943	0.914–0.973	0.000	0.936	0.902–0.971	0.000
ST elevation resolution (complete as reference):						
None	1.077	0.475–2.442	0.320			
Partial	0.576	0.261–1.270	0.083			
Symptom duration (1 hour increase)	1.014	0.944–1.088	0.710			
Angiographic and procedural						
Culprit artery (LAD vs. RCA and Cx)	1.726	0.402–7.417	0.250			
Initial TIMI flow (TIMI III as reference):						
0	1.747	0.597–5.114	0.750			
I	3.030	1.093–8.400	0.038			
II	1.146	0.359–3.655	0.530			
Thrombus after reclassification (grade TIMI V as reference):						
0	0.166	0.029–0.958	0.035			
I	0.243	0.062–0.954	0.770			
II	0.113	0.025–0.524	0.146			
III	0.318	0.079–1.286	0.956			
IV	0.484	0.150 – 1.554	0.206			
Glycoprotein IIb/IIIa inhibitors use	1.031	0.541–1.965	0.926			
Aspiration thrombectomy	0.837	0.405–1.730	0.230			
Final TIMI flow (TIMI III as reference):						
0	2.077	0.400–10.305	0.711			
I	2.760	0.828–9.206	0.429			
II	2.051	0.716–5.870	0.850			
MBG (grade III as reference):						
0	3.017	0.844–10.775	0.280			
I	2.007	0.744–5.413	0.407			
II	1.080	0.485–2.407	0.298			
AVDE	1.295	0.540–3.106	0.561			
Procedural success	0.741	0.377–1.458	0.385			
cTFC (1 Frame/s increase)	1.010	0.999–1.022	0.074	1.002	0.988–1.015	0.822
QuBE (1 unit increase)	0.923	0.864–0.985	0.016	0.919	0.846–0.999	0.049

AVDE — angiographically visible distal embolization; AUC — area under the curve; CI — confidence interval; CK-MB — creatine kinase muscle-brain isoenzyme; cTFC — corrected TIMI frame count; HR — hazard ratio; LAD — left anterior descending artery; Cx — circumflex artery; LVEF — left ventricular ejection fraction; MBG — myocardial blush grade; QuBE – quantitative blush evaluator; RCA — right coronary artery; TIMI — Thrombolysis in Myocardial Infarction

scale studies, the percentage of patients with previous MI or having been classified in Killip ≥ 2 class is relatively low [27], though patients with single vessel disease account one third of all STEMI patients [28]. These conditions explain the limited number of participants, but also enable an undisturbed interpretation of outcomes for this proof-of-concept study. To avoid doubt resulting from incomplete or staged revascularization in patients with multivessel coronary artery disease [29, 30]. The major difference between this study group and populations from other trials is the remarkably longer symptom duration time [27–30]. A considered opinion is that longer ischemic time translates to slightly lower QuBE score values in this study population in comparison to the population from the index study [18].

In contrast to the majority of contemporary trials evaluating interventional treatment of STEMI, which are reporting outcomes like death, re-infarction, and target lesion revascularization, this study focused on HF development as a primary study outcome. Data was provided by the NHF. These data were confirmed from archive data of index hospitalizations and were completely consistent. The diagnosis of HF during index hospitalization was made on the basis of HF symptoms and/or requirements for diuretic/inotropic treatment. According to consistency of our source data with data received from NHF, it was assumed that ICD-10 code I50.0–I50.9 will reflect the development of HF. Of course, such a method of outcome assessment might be a source of error, but it must be stressed that the proof-of-concept nature of this study and the in-person prospective follow-up of patients to control for the mildest symptoms of HF is recommended. Based on theseassumptions, approximately 40% incidence of HF in 36-months long follow-up were reported. This is an average result in comparison to the 25–56.3% incidence reported by Araszkiewicz et al. [1] 6-months long follow-up and 7.8% incidence reported by Carrick et al. [31] in a median follow-up of 845 days. Higher incidence of HF development in this study in comparison to the Carrick study, may be attributed to older age, more than a twofold longer time from onset of symptom to reperfusion, and a twofold lower administration rate of GP IIb/IIIa inhibitors in our population. Of note, we have to be aware of differences in diagnostic criteria of HF.

Of the many demographic, clinical, angiographic, and procedural variables only few remained significant predictors of HF development in the present study population. Kelly et al. [32] in the sub-analysis of the HORIZON-AMI trial have identified following determinants of new onset HF: previous MI, female sex, and LV systolic dysfunction, with insulin-requiring diabetes mellitus as a borderline correlate.

Of note, none of the well-established angiographic or procedural factors was associated with HF development in that report. Only after detailed analysis of the impact of diabetes on myocardial perfusion, from the CADILLAC study, a tentative conclusion was formulated that the diabetic population is more likely to have impaired myocardial perfusion, which may contribute to adverse outcomes [33]. This conclusion was approached upon comparable use of procedural resources (GP IIb/IIIa inhibitors, percentage of stents implanted) and percentage of patients with final TIMI III flow achieved. Comparing the stent use in our study with large scale randomized studies [34], it is substantially lower, though in comparison to registries [35, 36] it was at a similar level. In the same way, comparing the rate of final TIMI III flow reported herein, it is likewise with the 77% – 85% – 93% TIMI III flow rate reported by Vogelzang et al. [18] in respective subgroups, though there are reports on even 95% rate of TIMI III flow post-percutaneous coronary intervention [37].

Future perspective

The present results support the idea of another novel prognostic and therapeutic application of QuBE. It has already been shown to predict independently all-cause and cardiovascular mortality at 12 months [18]. It was also used by Porto et al. [38] to correlate microvascular obstruction with embolization of coronary circulation with platelet- and endothelial cell-derived microparticles, while Gu et al. [20] have indicated that QuBE is independent predictor of improved functional recovery of LV. As QuBE software requires only one cine-loop for reliable, operator-independent assessment of myocardial perfusion itappears to be a perfect tool for testing of adjunctive therapies aiming at improved myocardial perfusion. As its assessment can be repeated within a few minutes it may be suggested for testing drugs with vasoactive capabilities, locally delivered GP IIb/IIIa inhibitors, or procedures like ischemic post-conditioning. Improved QuBE score values after adjunctive treatment might be indicative of therapeutic efficacy and of improved outcome.

Limitations of the study

The major limitation of this study is the retrospective nature and relatively small number of

patients. A larger number of patients and larger number of complete cases would improve statistical significance. There is no information on other outcomes or clinical events such as stent thrombosis, in-stent restenosis, re-infarction, or cardiogenic shock. As re-infarctions might lead to a new onset HF, the information on stent thrombosis, in-stent restenosis, target lesion revascularization would provide more details on the mechanisms of HF development in follow-up. Long inclusion period and the changes in the AMI treatment along this period may also be a confusion factor. However, the long recruitment period pertains to the entire population of 1469 STEMI patients. This peculiar study population of 95 patients was actually enrolled during a much shorter period of time: from 2010 (1 patient) through 2013. Indeed, during 10 years of patient enrollment remarkable changes in AMI treatment have occurred: from wider implementation of GP IIb/IIIa use, through introduction of manual thrombus aspiration, and ending up with 100% use of drug eluting stent treatment, which was only recently implemented. The interventional treatment of STEMI patients, carried out in the middle period of the entire enrollment time is rather constant without extreme variabilities.

Conclusions

The QuBE assessment of myocardial perfusion allows the prediction of HF development in the post-infarction period in this highly selective group of patients. Before wider application of QuBE for therapeutic and prognostic purposes a clear definition of long-term outcomes should be established. Moreover, more studies including broader clinical presentation of patients are required.

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