

Thesis for doctoral degree (Ph.D.)
2017

From the Department of Clinical Science and
Education, Södersjukhuset, Karolinska Institutet.

Epidemiology and emergency cardiac care services for
Out-of-hospital cardiac arrest
in Qatar

FURQAN BIN IRFAN

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ISBN 978-91-7676-690-3

Printed by E-Print AB 2017

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THESIS FOR DOCTORAL DEGREE (Ph.D.)

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ABSTRACT

Background:

Out-of-hospital cardiac arrest (OHCA) is a common cause of cardiac emergency and death. Worldwide, there is wide variation in epidemiology and survival of OHCA. Racial and ethnic disparities are important contributors towards such variation. OHCA is mostly cardiac in origin, however there are several other non-cardiac etiologies of OHCA including trauma, submersion, drugs intoxication, asphyxia, conflagration, electrocution. With increasing trauma burden, traumatic cardiac arrest (TCA) is becoming more common. There are limited population-based studies on OHCA in the Asian region.

Aim:

The aims were to establish a national OHCA registry and determine the epidemiology, prehospital interventions, emergency management and outcomes of OHCA of cardiac and non-cardiac origin, with focus on TCA. Since Qatar, has a high trauma burden, TCA studies are feasible, important for public health and serve as important benchmarking indicators for EMS, cardiac and trauma services.

Methods:

Utstein based guidelines were followed for data collection on prospectively enrolled OHCA patients resuscitated by EMS for establishment of OHCA registry, in Qatar, from June 2012 to May 2015. Study I and II, utilized data from the OHCA registry, while Study III and IV also utilized data from the Trauma registry, in Qatar.

Study I was a nationwide population-based study that analyzed OHCA registry patients to describe epidemiology, cardiac arrest features, emergency management, health services delivery and outcomes.

Study II was a retrospective cohort study that compared epidemiology, clinical presentation, emergency management, health services delivery and outcomes between Middle Eastern Gulf Cooperation Council (GCC) Arab ethnic and North African ethnic OHCA patients.

Study III was a nationwide population-based observational study that analyzed out-of-hospital traumatic cardiac arrest (OHTCA) patients utilizing the OHCA registry and Trauma registry.

Study IV was a retrospective cohort study that redefined TCA in two distinct categories and compared in-hospital traumatic cardiac arrest (IHTCA) patients with OHTCA patients.

Results:

In *Study I*, the age-sex incidence of cardiac origin OHCA resuscitated by EMS was 87.8 per 100,000 population. Of the 447 OHCA patients analyzed, bystander cardiopulmonary resuscitation (CPR) rate was 20.6% and survival rate was 8.1%. In multivariable regression analysis, survival was associated with initial shockable rhythm (OR 13.4, 95% CI 5.4–33.3), male gender (OR 0.27, 95% CI 0.1–0.8) and advanced cardiac life support (ACLS) (OR 0.15, 95% CI 0.04–0.5).

In *Study II*, there were 285 Middle Eastern GCC Arab ethnicity OHCA patients compared with 112 North African ethnicity OHCA patients, in Qatar. Multivariable regression analysis model showed that North African OHCA patients were associated with initial shockable rhythm (OR 2.86, 95% CI 1.30-6.33), greater scene time (OR 1.02 95% CI 1.0-1.04) and diabetes (OR 0.48, 95% CI 0.25- 0.91).

In *Study III*, the mean annual crude incidence rate of OHTCA patients was 4.0 per 100,000 population, in Qatar. Of 410 OHTCA patients, majority had blunt injuries (94.3%) with survival rate of 2.4%. Multivariable regression analysis for return of spontaneous circulation (ROSC) showed association with initial shockable rhythm (OR 6.4, 95% CI 1.3-30.7), external hemorrhage control (OR 5.9, 95% CI 1.9-18.0), and prehospital needle thoracostomy (OR 5.3, 95% CI 1.3-21.7). Univariate analysis for survival to hospital discharge showed association with initial shockable rhythm (OR 10.12, CI 0.97–105.23), Adrenaline (OR 0.045, CI 0.006–0.358), external hemorrhage control (OR 4.2, CI 1.03–16.8), blood transfusion (OR 9.22, CI 2.5–33.7) and surgery (OR 32.1, CI 7.54 136.6)

In *Study IV*, there were 410 OHTCA patients compared with 199 IHTCA patients, in Qatar. The mean annual crude incidence of IHTCA was 2.0 per 100,000 population with a survival rate of 7.5%. In multivariable regression analysis, IHTCA was associated with cardiac re-arrest (OR 6.0, 95% CI 3.3-10.8, $p < 0.00$), abdominal injury (OR 2.0, 95% CI 1.0-3.8), spinal injury (OR 3.5, 95% CI 1.5-8.3), higher prehospital GCS (OR 1.4, 95% CI 1.4-1.6) and survival (OR 6.3, 95% CI 1.3-31.2).

Conclusions:

Standardized OHCA incidence and survival rates were comparable to industrialized countries but bystander CPR and defibrillation rates can be improved with tailored public education and training programs.

North African OHCA patients were younger, associated with less risk factors, greater shockable rhythm, and received greater ACLS interventions with higher median EMS scene time compared to GCC Arab OHCA patients.

Incidence of OHTCA was comparatively less than international rates and disproportionately low, relative to the trauma burden, in Qatar. Prehospital and emergency department (ED) management; hemorrhage control, needle thoracostomy, blood transfusion and surgery, were beneficial for survival and intervention studies are required to further guide management.

IHTCA was a new sub-category of traumatic cardiac arrest that was defined and was associated with greater cardiac re-arrest, mean GCS score, initial shockable rhythm, and survival rates compared to OHTCA.

LIST OF ORIGINAL PUBLICATIONS

- I. Irfan FB, Bhutta ZA, Castren M, Straney L, Djarv T, Tariq T, Thomas SH, Alinier G, Al Shaikh L, Owen RC, Al Suwaidi J, Shuaib A, Singh R, Cameron PA.
Epidemiology and outcomes of out-of-hospital cardiac arrest in Qatar: A nationwide observational study.
International Journal of Cardiology 2016 Nov 15;223: 1007-1013.
- II. Irfan FB, Castren M, Bhutta ZA, George P, Qureshi I, Thomas SH, Pathan SA, Alinier G, Al Shaikh L, Al-Suwaidi J, Singh R, Shuaib A, Tariq T, McKenna WJ, Cameron PA, Djarv T
Ethnic differences in out-of-hospital cardiac arrest resuscitation among Middle Eastern Arabs and North African populations living in Qatar.
- III. Irfan FB, Consunji R, El-Menyar A, George P, Peralta R, Al-Thani H, Thomas SH, Alinier G, Shuaib A, Al-Suwaidi J, Singh R, Castren M, Cameron PA, Djarv T
Cardiopulmonary resuscitation of out-of-hospital traumatic cardiac arrest in Qatar: A nationwide population-based study.
International Journal of Cardiology (2017), doi: 10.1016/j.ijcard.2017.03.134
- IV. Irfan FB, Consunji R, Peralta R, El-Menyar A, George P, Dsouza L, Al-Thani H, Thomas SH, Alinier G, Shuaib A, Al-Suwaidi J, Singh R, Castren M, Cameron PA, Djarv T
In-hospital traumatic cardiac arrest.

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LIST OF ABBREVIATIONS

OHCA	Out-of-hospital cardiac arrest
EMS	Emergency Medical Services
OHTCA	Out-of-hospital traumatic cardiac arrest
IHTCA	In-hospital traumatic cardiac arrest
ROSC	Return of spontaneous circulation
IHCA	In-hospital cardiac arrest
CPR	Cardiopulmonary resuscitation
TCA	Traumatic cardiac arrest
OHTCA	Out-of-hospital traumatic cardiac arrest
IHTCA	In-hospital traumatic cardiac arrest
GCC	Gulf Cooperation Council
MVA	Motor vehicle accidents
SA	Sinoatrial
RCA	Right coronary artery
LCA	Left coronary artery
AV	Atrioventricular
US	United States
VF	Ventricular fibrillation
pVT	Pulseless ventricular tachycardia
SD	Standard deviation
CPC	Cerebral Performance Category
ED	Emergency department
HTN	Hypertension
DM	Diabetes mellitus
EF	Ejection fraction
AED	Automated external defibrillator
ILCOR	International Liaison Committee on Resuscitation
AHA	American Heart Association
BLS	Basic life support
ACLS	Advanced cardiac life support
ALS	Advanced life support
IV	Intravenous
PAD	Public access defibrillation
RCT	Randomized controlled trial
STEMI	ST elevation myocardial infarction
NSTEMI	Non-ST elevation myocardial infarction
MAP	Mean arterial pressure
EEG	Electroencephalography
ROC	Resuscitation Outcomes Consortium
TBI	Traumatic brain injury
SBP	Systolic blood pressure
GCS	Glasgow Coma Scale
HMC	Hamad Medical Corporation
CARES	Cardiac Arrest Registry to Enhance Survival

CDC	Centers for Disease Control
IRB	Institutional Review Board
HMCAS	Hamad Medical Corporation Ambulance Services
EMR	Electronic medical record
RTA	Road traffic accident

1 INTRODUCTION

Cardiac arrest is an emergency that annually affect millions of people globally.¹ It is sudden cessation of cardiac activity that causes termination of blood flow circulation leading to sudden hemodynamic collapse.³ Based on the etiology, cardiac arrest can be divided into cardiac and noncardiac origin. Majority of the cardiac arrests are of cardiac origin with coronary artery disease and previous heart disease being the primary etiology.² Noncardiac origin cardiac arrest can be caused by trauma, submersion, conflagration, electrocution, drugs intoxication, asphyxia or other noncardiac etiology.³

OHCA is different from in-hospital cardiac arrest (IHCA) depending on the location of the cardiac arrest victim. OHCA is cardiac arrest that occurs outside a hospital or healthcare setting while IHCA occurs in hospital setting. TCA is cardiac arrest in a trauma patient that causes cessation of cardiac activity and termination of blood flow circulation leading to hemodynamic collapse.⁴ OHTCA has been defined previously as prehospital cardiac arrest in a trauma patient.⁴

There is wide variability in reported OHCA incidence and survival rates. Incidence of EMS-assessed OHCA in United States was 110.8 per 100 000 population.³ Ethnicity and race-based healthcare disparities have a role in the variation of OHCA, especially for outcomes and survival.⁵⁻¹⁰ There are limited nationwide population-based studies on OHTCA; incidence of 6.0 per 100,000 was reported in Australia.¹¹

In case of an OHCA, immediate time-dependent life-saving interventions are required by the lay persons in community and EMS.³ The emergency series of interventions is termed ‘Chain of survival’ and include EMS activation, bystander cardiopulmonary resuscitation (CPR), defibrillation, advanced cardiac life support (ACLS) by EMS and post-resuscitative care.³

For TCA, besides CPR and ACLS additional emergency measures for management of trauma need to be undertaken; airway placement, external hemorrhage control, splints, intravenous fluids, chest decompression, thoracotomy, blood transfusion and surgery.⁴

Outcomes following OHCA have improved over past few decades with better emergency health systems and community CPR training and preparedness.³ Survival to hospital discharge of EMS-assessed non-traumatic origin OHCA in US was 12%.³ Although historically survival of OHTCA have been poor, recent studies have reported survival rates at 5.6–7.5%.¹¹⁻¹⁴

2 RATIONALE

OHCA is a major public health problem and affects millions of people globally. It is a challenge for emergency care systems due to the high mortality rate and the logistics of providing the immediate treatment required. Understanding the epidemiology, pre-hospital emergency care and outcomes for OHCA patients is important for identifying high-risk populations and identifying community preparedness and EMS requirements.

Over past few decades, there has been massive development and huge influx of expatriates in Qatar.¹⁵ Local Qatari population represent a small segment of the total population, with over 80% of the population being expatriates/immigrants.^{15,16} The differences in epidemiology, cardiac arrest features, management and survival of OHCA among ethnicities, local GCC Arabs in comparison with immigrant patients, may lead to improvements in emergency health services and changes in health policy for better outcomes. Differences in epidemiology and risk factors of OHCA between ethnicities can help to target preventive measures, such as enhanced screening for cardiac diseases, for ethnicities at increased risk of cardiac arrest. Differences in “chain of survival,” (CPR and defibrillation rates) between the ethnicities will help identify ethnic disparities in OHCA awareness and CPR training in the communities. Moreover, differences between the ethnicities in EMS-time intervals and health service delivery will assess healthcare disparities and equity, in Qatar.

Qatar’s rapid progress has also caused a huge trauma burden.¹⁵ The major contributors to the trauma burden, in Qatar are occupational injuries and road traffic accidents.^{15,16} The increased number of traumatic injuries would also lead to an increased incidence of TCA. The etiology, pathophysiology, management and outcomes of TCA patients are very different from medical or cardiac origin cardiac arrest. Survival of OHTCA patients have improved markedly with better pre-hospital and emergency management over past few decades and some studies now report survival rates equal to medical or cardiac origin cardiac arrest.¹⁷⁻²⁰ With massive construction industry employing over a million people and a high rate of motor vehicle accidents (MVAs) in Qatar, it is important to determine the epidemiology and outcomes of OHTCA.^{15,16} Results of OHTCA in Qatar will have implications for other rapidly developing countries with huge trauma burden.

Although prehospital or OHTCA has been well defined there are no studies on delayed cardiac arrest following trauma. OHTCA includes cardiac arrest following primary traumatic injury causing cardiac arrest and secondary traumatic event, as a result of primary cardiac arrest. However, delayed traumatic cardiac arrest occurring in-hospital, only includes cardiac arrest following traumatic injury. It would be important to distinguish IHTCA from OHTCA and determine the epidemiology, injury mechanisms, clinical presentation and pathophysiology for delayed cardiac arrest in IHTCA. This could lead to better understanding of OHTCA and IHTCA and guide management for improved outcomes in patients.

3 AIMS

The overall goal of the current work is to determine the epidemiology, etiology, risk factors, emergency processes, community intervention, management and outcomes, of cardiac and traumatic origin OHCA, in Qatar.

Additional and constituent study-specific aims were:

To describe OHCA epidemiology, risk factors, cardiac arrest features (witnessed arrest, bystander CPR and defibrillation, initial shockable rhythm), pre-hospital emergency management (time-related indicators, pre-hospital advanced life support), and outcomes, and determine the factors that predict OHCA outcomes; ROSC and survival, in Qatar

Comparison of OHCA epidemiology, risk factors, cardiac arrest characteristics pre-hospital emergency management and survival between the local Middle Eastern GCC Arab ethnicity OHCA patients and the expatriate North African ethnic OHCA patients, living in Qatar.

To describe OHTCA epidemiology, cardiac arrest and trauma characteristics, pre-hospital interventions, emergency department (ED) management, and outcomes, and determine the factors associated with OHTCA outcomes; ROSC and survival, in Qatar

To describe IHTCA epidemiology, cardiac arrest features, trauma characteristics, anatomical injury pattern and outcomes, in Qatar. Comparison of IHTCA and OHTCA epidemiology, cardiac arrest features, trauma characteristics, anatomical injury pattern, pathophysiology and outcomes.

4 RESEARCH QUESTION AND HYPOTHESIS

- Study I* What is OHCA epidemiology, risk factors, cardiac arrest features, pre-hospital emergency management and outcomes in Qatar.
- Study II* The null hypothesis was that there was no difference in epidemiology, clinical presentation and outcomes between the local, Middle Eastern GCC Arab ethnic OHCA patients, and the expatriates, North African ethnicity OHCA patients, living in Qatar.
- Study III* What is OHTCA epidemiology, cardiac arrest and trauma characteristics, pre-hospital interventions, emergency department (ED) management, and outcomes in Qatar.
- Study IV* The null hypothesis was that there was no difference in epidemiology, clinical presentation, pathophysiology, cardiac arrest and trauma characteristics, and outcomes between OHTCA and IHTCA patients, in Qatar.

5 OUT-OF-HOSPITAL CARDIAC ARREST

5.1 DEFINITION

OHCA is defined as termination of cardiac contraction that is evident by unconsciousness, loss of pulse and breathing, and that takes place outside of a hospital setting.^{3,21-23} Most studies include OHCA patients who receive resuscitative attempts by EMS or bystander, while those with clear signs of death are excluded.³

5.2 EPIDEMIOLOGY

Globally, there is wide variability reported in epidemiology of OHCA. An estimated 356 500 people in the United States (US) suffer Emergency Medical Services (EMS)-assessed OHCA annually, of which 347 000 are adults.³ A global OHCA study in 2010, reported the incidence of EMS-resuscitated OHCA of cardiac origin in Europe, North America and Asia was 35, 54.6 and 28.3 per 100,000 person-years, respectively.²⁴ The average incidence globally of adults with cardiac origin OHCA was 55 per 100,000 person years.²⁴

Regional variability in epidemiology of OHCA can be estimated by the incidence of EMS-assessed cardiac origin OHCA per 100,000 person-years in Europe; Vienna (49.7), Copenhagen (28.3), London (47.0), Estonia (25.9), Helsinki (49.4), Amsterdam (35.8), Edinburgh (45.0) and Heidelberg (34.1).²⁴ Within country variability is indicated by the incidence of EMS-assessed cardiac origin OHCA per 100,000 person-years in United States; Dallas (63.6), Houston (92.1), Detroit (148.8), Los Angeles (66.2), New York (52.3), San Francisco (82.2) and Pittsburgh (61.4).²⁴ Incidence of 63.6 in Dallas and 92.1 in Houston per 100,000 person-years, in the State of Texas within driving distance of 4 to 5 hours cannot be explained by differences in populations and disease processes. Artificial variability explained by Berdowski et al., could be due to difference in EMS systems, difference in data collection methods, and OHCA patient definitions and population denominator.²⁴

Most of the OHCA occur at home (65-70%).^{3,4,25} Other locations of OHCA include nursing home/assisted facility (13.5%), public building (5.9%), street/highway (4.8%), recreation facility (1.3%) and industrial place (0.7%).³ Around 15-20% of OHCA occur in public place.^{26,27}

The mean age of EMS-assessed cardiac origin OHCA was 64 years, standard deviation (SD \pm 18.2), in US.³ Gender plays a role in OHCA with men having higher incidence than women.²⁸ There were 61.1% male, EMS-assessed cardiac origin OHCA patients in US.³ The difference in incidence between genders peaks in middle-age and decreases thereafter which may be related to postmenopausal increased risk of cardiac diseases in females.²⁸ A recent meta-analysis showed that women were older and had a greater likelihood of having OHCA at home.²⁹

Racial and ethnicity differences in OHCA have mainly been studied in western countries, comparing African Americans with Caucasians.³⁰⁻³³ African Americans have a higher incidence of OHCA compared to Caucasians.³¹ OHCA CARES registry in US, reported that 26.9% OHCA patients were African Americans, 5.3% were Hispanic/Latino and 38.9% were Caucasians.³

5.3 ETIOLOGY

There are many etiologies that can lead to an abnormal cardiac rhythm causing cardiac arrest, including ischemic heart disease, cardiomyopathy, inherited and congenital heart defects and structural changes in the heart (congestive heart failure, valvular defects, infiltrative diseases, myocarditis).² Cardiac etiology accounts for 70-85% of OHCA, while non-cardiac etiology has been reported to cause 20-40% of OHCA.³⁴ Non-cardiac origin OHCA have various etiologies including trauma, submersion, drug-intoxication, asphyxia, electrocution, respiratory diseases etc.³

5.4 PATHOPHYSIOLOGY

The electrical impulses of the cardiac conducting system causing rhythmic contraction, originate from the sinoatrial (SA) node in the right atrium of the heart. The blood supply to SA node is via the SA nodal artery which in turn is supplied by the right coronary artery (RCA) (55% to 63%), it can also be supplied by circumflex branch of left coronary artery (LCA) (37% to 45%).³⁵⁻³⁷ Electrical impulses originating from the SA node are conducted to the atrioventricular (AV) node situated in the interatrial septum, which then spread through the right and left bundle of His and Purkinje fibres to cause contraction of the heart and pump blood to the rest of the body.³⁶ The AV node and His bundle is supplied by the AV node artery which originates from RCA (90%) in most cases, and LCA (10%) in the remainder.³⁷

Acute cardiac ischemia and infarction are the commonest cause of cardiac arrest.² Atherosclerosis from plaque formation in coronary arteries leads to occlusion and results in myocardial ischemia that progresses to infarction and necrosis of the SA and AV node, and the conducting system pathway causing disruption in the rhythm and electrical conduction leading to life-threatening arrhythmias.³⁵ Anteroseptal infarcts due to blockage of left anterior descending coronary artery usually do not lead to atrial arrhythmias since blood supply to SA node and AV node is not compromised.³⁶ Lateral infarcts because of left circumflex artery occlusion can lead to heart block in 10% of the patients where it supplies the AV node and bundle of His, and atrial arrhythmias in 37% to 45%, of the patients where it supplies the SA node.³⁶ Arrhythmias from ischemia or infarction of SA node include sinus bradycardia/ arrest, atrial block and bradycardia/ tachycardia.³⁵ Posterior infarcts as a result of RCA occlusion, can cause AV blocks especially since it supplies the AV node, and His bundle.³⁶

The usual sequence of arrhythmias in cardiac arrest originates from ventricular tachyarrhythmias (65% to 80%) progressing to ventricular fibrillation and eventually deteriorating to

asystole.^{2,35,38,39} Bradyarrhythmia can also be the primary abnormal rhythm accounting for 5% to 20%, of cardiac arrest patients.³⁵

5.5 RISK FACTORS

Heart disease is a major risk factor for OHCA. Studies have reported that in greater than 50% of the patients, the first presentation of heart disease was a cardiac arrest.^{25,40} Risk factors for cardiac arrest include hypertension (HTN), hypercholesterolemia, obesity, glucose intolerance/ diabetes mellitus (DM), family history of heart diseases, smoking, male gender, and advanced age.^{28,41-44} Other prognostic risk factors include left-ventricular dysfunction (left ventricular ejection fraction \leq 30-35), left-ventricular hypertrophy, ECG abnormalities, functional class, previous heart failure/ myocardial infarction, tachycardia and atrial fibrillation.^{28,45-49} Currently, only heart disease patients with left ventricular ejection fraction \leq 30-35, are taken as high-risk for cardiac arrest and recommended prophylactic implantable cardioverter-defibrillator (ICD).^{47,50,51}

5.6 CLINICAL PRESENTATION

The signs and symptoms of cardiac arrest include a sudden loss of consciousness (fainting), hemodynamic collapse and loss of pulse, and loss of breathing or agonal breaths.⁵² Cardiac arrest due to cardiac conduction abnormalities is often confused with heart attack that results from occlusion of coronary arteries.⁵² Heart attack signs and symptoms include chest pain, neck/jaw/arms/back pain, shortness of breath, nausea and vomiting, diaphoresis and light-headedness or dizziness.⁵² A heart attack from occlusion of coronary artery can cause ischemia of cardiac conduction system and lead to cardiac arrest, but it cannot happen the other way around.⁵² It is important to distinguish between cardiac arrest and heart attack because community intervention and emergency management is vastly different.

5.7 COMMUNITY INTERVENTION

Interventions to improve survival for OHCA patients include early EMS activation, and bystander CPR and defibrillation, facilitating EMS performed pre-hospital pharmacological and other resuscitative measures, and continued resuscitation and post-resuscitative care at the receiving hospital.⁵³⁻⁵⁷ The probability of surviving an OHCA can increase significantly, if EMS paramedics or bystanders immediately intervene in a sequence of actions called the “chain of survival.” Urgent actions include a) rapid EMS activation by calling the appropriate emergency response number, b) immediate initiation of CPR, c) rapid use of automated external defibrillator (AED) as required, d) Pre-hospital EMS advanced life support management, e) post-resuscitative management.³

Utstein guidelines provide a uniform method for collecting and reporting OHCA data.^{21,58} Utstein template categorizes witnessed arrest into unwitnessed, bystander witnessed and witnessed by EMS staff.³ Around 50% of OHCA are unwitnessed.⁵⁹ Witnessed cardiac arrest is important since it leads to greater likelihood of bystander CPR and initial shockable rhythm and is an independent predictor of improved survival in OHCA.⁶⁰⁻⁶²

Early recognition of OHCA signs and symptoms (sudden collapse, loss of pulse, loss of breathing/gasping agonal breaths) by a bystander (lay responder) is critical for activation of EMS and to start bystander CPR and perform defibrillation by utilizing AED, till EMS personnel arrive.⁵⁹

The chest compressions in CPR mechanically acts as a pump to circulate blood flow while the rescue breaths provide oxygenation for achievement of sustained ROSC.⁵² Early bystander CPR during cardiac arrest is essential for increased odds of survival and neurological function.^{62,63} Bystander CPR is associated with increased shockable rhythm and decreased number of defibrillation shocks to achieve ROSC and increased survival rates.⁶⁴ Recent guidelines recommend that untrained lay rescuer should provide chest compression-only CPR (without rescue breaths) with chest compressions of 100 to 120/min, trained lay rescuer should at least perform chest compressions and if possible should add rescue breaths (mouth to mouth ventilation) with ratio of 30 compressions: 2 breaths per minute.⁵⁹ The chest compression-depth should be between 2 inches (5 centimeters) to 2.4 inches (6 centimeters).⁵⁹

Telephone-CPR instructions by EMS dispatcher leads to increased bystander CPR performance and improved survival rates.⁶⁵ Dispatchers are recommended to provide chest-compression only CPR instructions to lay person.⁵⁹

Further Utstein stratification is by first cardiac arrest rhythm recorded on defibrillator or monitor; shockable (ventricular fibrillation [VF] and pulseless ventricular tachycardia [pVT]), and non-shockable (pulseless electrical activity and asystole).³ VF could arise from ischemia in the conduction pathway resulting in uncoordinated contraction of myocardium, while pVT causes extremely fast heart rate without ventricular contraction.⁵² In pulseless electrical activity, electrical impulses are present but it does not illicit cardiac contraction, while in asystole there is no electrical activity.⁵²

Shockable rhythms; VF and pVT, can be managed by immediate defibrillation and can revert to normal rhythm while non-shockable rhythm cannot usually be defibrillated.⁵² An AED is a portable device that can recognize a cardiac rhythm, provide electrical shock and advise whether to give shock in case of shockable rhythm or continue CPR if the rhythm is non-shockable.⁵² Basic life support (BLS) trained lay responders should promptly apply an AED on OHCA patient and perform defibrillation in case of shockable rhythm.⁵⁹ Bystander CPR and chest compressions should be started and continued till AED is available for defibrillation and resumed immediately after a shock.⁵⁹ Public access defibrillation (PAD) programs include training and provision of AED in public places for lay-responders to have immediate access, in case of OHCA. Guidelines recommend that PAD programs be implemented in public places.⁶⁶

Incidence of shockable rhythm indicating better survival chances, for OHCA occurring at home was 25% for EMS-witnessed arrest, 35% for bystander-witnessed and 36% for bystander-performed automated external defibrillators (AEDs).²⁷ Incidence of shockable rhythm for OHCA occurring in a public place were better in comparison with 38% for EMS-witnessed arrest, 60% for bystander-witnessed and 79% for bystander-performed automated external defibrillators (AEDs).²⁷

Minorities have a decreased likelihood to have witnessed arrest, receive bystander CPR and have an initial shockable rhythm.^{31,33} Women had less likelihood of witnessed OHCA and initial shockable rhythm and greater likelihood of receiving bystander CPR compared to men.²⁹

5.8 EMERGENCY MANAGEMENT

Advanced life support (ALS) or ACLS is provided by paramedics and health professionals for advanced resuscitative emergency management of OHCA and IHCA. Even though ALS/ACLS is widely implemented in emergency management of cardiac arrest, its benefits in improving OHCA survival are controversial.⁵² Previous studies have demonstrated similar survival rates in patients who received BLS or ALS.⁶⁷ A recent study showed that OHCA patients who received BLS had better survival to hospital discharge, survival at 90 days, and neurological function compared to patients who received ALS.⁶⁸ However, a meta-analysis reported that ALS resulted in increased survival rate compared to BLS in OHCA patients.⁶⁹

ALS/ACLS guidelines for cardiac arrest management includes CPR and defibrillation, airway (ie, endotracheal intubation, supraglottic airway device) and bag-mask ventilation, intravenous (IV) and intraosseous access, administration of anti-arrhythmic drugs (eg. amiodarone) and vasopressors (epinephrine), physiologic monitoring and hemodynamic support.^{52,70,71} Updated ALS/ACLS guidelines include the following: emphasis on continuous chest compressions during CPR (with interruptions ≤ 5 seconds for defibrillation or intubation); supplementary oxygen administration if available; utilization of ultrasound (if it does not interfere with CPR); waveform capnography utilization (to confirm endotracheal tube placement, monitor ventilation rate/ CPR quality and ROSC detection); 10 breaths per minute post-airway placement; use of mechanical chest compression device (where manual chest compressions are impractical); and extracorporeal CPR (ECPR) in selected patients.^{66,71}

Post-resuscitation care should be immediately initiated once ROSC is achieved.⁷¹ Post-cardiac arrest syndrome is a complex disorder affecting multiple organ systems that develops after ROSC is achieved.^{72,73} The post-cardiac arrest multi-organ system pathology involves brain injury, myocardium dysfunction, ischemia and reperfusion of tissues causing a shock condition similar to sepsis and pre-existing cardiovascular pathology.⁷² Immediate efforts to correct post-ROSC hypotension should be avoided.⁷⁴

Previous studies showed that therapeutic hypothermia between 32 to 34 degrees Celsius for 12 to 24 hours, in post-cardiac arrest unconscious/comatose patients improved survival and neurological function.^{56,57} Guidelines in 2010, recommended that unconscious/comatose OHCA patients with VF/pVT rhythm and ROSC should undergo therapeutic hypothermia of 32 to 34 degrees Celsius for 12 to 24 hours.⁷⁵ However, some studies have questioned whether improvements in outcomes were due to hypothermia or prevention of fever, since fever in cardiac arrest survivors has been associated with poor outcomes.⁷⁶⁻⁷⁸ A recent large randomized controlled trial (RCT) of 939 OHCA patients showed that there was no difference in outcomes between hypothermia at 33 degrees Celsius and targeted temperature at 36 degrees Celsius.⁷⁷ Recent guidelines recommend that targeted temperature management should be implemented in OHCA patients for at least 24 hours between the range of 32 to 36 degrees Celsius.^{74,79} Hypothermia post-ROSC with infusion of cold fluids was advised against.^{74,79}

Other post-resuscitation care measures include diagnosis of seizures by electroencephalography (EEG) and standard management by anticonvulsants, oxygenation to avoid hypoxia, and maintaining carbon dioxide within normal physiological range.⁷⁴ Guidelines recommend that emergency coronary angiography and intervention as indicated should be performed for OHCA

patients with ST elevation myocardial infarction (STEMI) and for select unstable OHCA patients with acute coronary syndrome and non-ST elevation.⁷⁴

5.9 OUTCOMES

Outcomes for OHCA include ROSC defined as restoration of pulse/ blood pressure, survival to hospital admission and discharge, 30 days after discharge, and longer term survival after 1 year and 3 years, etc. Neurological function post-arrest is generally determined by using a measuring scale like the Cerebral Performance Category (CPC) score.⁸⁰

Like incidence, there is wide variability in outcomes of OHCA. In a recent PAROS study, which is a consortium of Pan-Asian Resuscitation Outcomes Study, EMS ROSC for non-traumatic EMS-resuscitation attempted OHCA cases were 8.8% for Japan, 5.0% for Korea, 3.4% for Malaysia, 5.1% for Singapore, 21.0% for Thailand, 12.8% for Taiwan and 3.6% for UAE.²⁵ In the same study, Emergency department (ED) ROSC were 37.4% for Korea, 8.3% for Malaysia, 26.1% for Singapore, 28.5% for Thailand, 30.5% for Taiwan and 5.9% for UAE.²⁵ Pre-hospital ROSC in US, for presumed cardiac origin EMS-resuscitation attempted OHCA patients was 34.4%.³

Survival to hospital admission were 28.5% for Japan, 22.7% for Korea, 5.9% for Malaysia, 16.6% for Singapore, 21.5% for Thailand, 24.0% for Thailand and 7.9% for UAE.²⁵ Survival to hospital admission was 26.3%, for US.³

Survival to hospital discharge were 5.6% for Japan, 9.9% for Korea, 1.0% for Malaysia, 2.5% for Singapore, 2.7% for Thailand, 4.8% for Taiwan and 2.8% for UAE.²⁵ Survival to hospital discharge for EMS-treated presumed cardiac origin in Europe was 10.7%. In US, survival to hospital discharge of EMS-assessed non-traumatic OHCA was 12%.⁴

Survival for witnessed arrest with VF was 31.2% for Japan, 29.6% for Korea, 9.7% for Singapore, 18.9% for Taiwan and 13.0% for UAE.²⁵ Survival for EMS-treated presumed cardiac origin VF rhythm OHCA in Europe was 21.2%.⁸¹ Survival for non-traumatic EMS-treated witnessed arrest with VF was 38.6%, in US.⁴

A favorable post-arrest neurological outcome of CPC score of 1 or 2 in non-traumatic EMS-resuscitation attempted OHCA patients were 3.1% in Japan, 3.7% in Korea, 1.6% in Singapore, 2.2% in Thailand, 2.9% in Taiwan and 2.6% in UAE.²⁵ In CARES registry in US, a favorable post-arrest CPC score was 6.9%.³

Variability in outcomes could be explained by different rates of bystander CPR and defibrillation, different EMS services, varying prehospital care and emergency protocols, and management.⁵²

Location of OHCA could lead to difference in survival rates, OHCA in public places with AED (34%) had greater survival rates than OHCA at home (12%).²⁷ Ethnicity also has a role in OHCA survival with African Americans having lower rates of survival compared to

Caucasians.³¹ Gender influences survival with women having greater survival at hospital discharge compared to men.²⁹ This could be due to female hormones having cardio- and neuroprotective role and stronger vagal response in women having anti-arrhythmic and reduced oxygen requirement in OHCA.²⁹

6 TRAUMATIC CARDIAC ARREST

6.1 Definitions

TCA was defined as termination of cardiac output in severely injured or trauma patient.^{4,82} Some studies have defined TCA as cardiac arrest in a trauma patient occurring in either prehospital phase or in ED/trauma room.^{19,83} Few studies, have also described TCA in the ED.^{12,84} However, most recent studies have reported and defined prehospital or OHTCA as a trauma patient having received CPR in pre-hospital phase.^{11,82}

6.2 Epidemiology

There are limited population-based studies on epidemiology of TCA. Moreover, very few studies have determined incidence of TCA. The incidence rate of OHTCA in Melbourne was 6.0 per 100,000 population.¹¹

Estimates of incidence derived from other studies report approximately 2 to 12 per 100 severe trauma patients will have a TCA.^{82,85} A study by Battistella et al., reported 604 TCA patients among 16,724 trauma patients that were admitted in level 1 trauma center, giving 3.6 TCAs for every 100 level 1 trauma patient admissions.⁸³ Another study by Stockinger et al., described 588 OHTCA patients in 16,651 trauma patients who met level 1 criteria, that is 3.53 OHTCA for every 100 level 1 trauma patients.⁸⁶ A recent study identifying OHTCA patients from Resuscitation Outcomes Consortium (ROC) registries in North America analyzed all severe trauma patients including those that died in the field, reported 2424 OHTCAs in 19,549 patients that equated to 12.4 OHTCAs per 100 severely injured trauma patients.⁸²

The mean age of traumatic arrest patients ranged from 39 years to 53 years.^{82,87} Males accounted for 74% to 79% of the traumatic arrest patients.^{11,12,82} The frequent mechanisms of trauma were motor vehicle collisions (MVC) (24% to 57%), gunshot injuries (17% to 26%) and falls (8% to 15%).^{11,82} Majority of traumatic arrest cases were due to blunt injuries (68% to 87%).^{82,84,88} Most of the OHTCA occurred on streets and roads (32% to 56%), followed by home (20% to 28%) and public places (9% to 17%).^{82,87,88}

6.3 ETIOLOGY

Cardiac arrest in a trauma patient has a very different etiology compared to cardiac arrest due to cardiac origin (OHCA). As opposed to cardiac etiology in OHCA, etiology in TCA mostly involves other systems:

- Cardiac etiology (ischemic heart disease, cardiomyopathy, inherited and congenital heart defects and structural changes in the heart) causing OHCA leading to secondary trauma.⁸⁹
- Trauma to the heart and major vascular trauma; aorta and pulmonary artery
- Hypovolemia due to massive blood loss in trauma

- Head injury leading to secondary cardiovascular deterioration
- Asphyxial cardiac arrest due to hypoxia in respiratory arrest, pneumothorax, obstruction or injury to the respiratory system.⁹⁰
- Pericardial tamponade/ tension pneumothorax by chest trauma.⁹⁰

A study by Georgescu et al., determined etiology of TCA to be hypovolemia (40.8%), severe head injury (32.8%), hypoxia (20.9%) and tension pneumothorax (5%).⁸⁴ This corresponds well with another study that reported the incidence of tension pneumothorax in TCA patients to be 5.7%.¹⁹ Approximately, 2.5% of OHCA's happen in a car, that can lead to a secondary traumatic event.⁸⁹ A study on deaths due to TCA analyzed many variables including autopsy data and concluded that TCA due to hypovolemia was 48%, tension pneumothorax was 13%, hypoxia was 13% and pericardial tamponade was 10%.⁹¹

6.4 PATHOPHYSIOLOGY

The pathophysiology of TCA is very variable and depends on the underlying etiology. For TCA caused by OHCA leading to secondary trauma, the pathophysiology for the cardiac event is similar as described in Chapter 5 for cardiac origin OHCA.

The heart and great vessels can be injured by direct blunt or penetrating trauma.⁹² The various mechanisms of injury include chest compression, direct injury, deceleration, traction or torsion and rupture.⁹² Commotio cordis is caused by chest injury during a critical phase of electrical conduction cycle which results in ventricular fibrillation.⁹³ Myocardial contusion results from direct blunt injury and leads to cardiac failure and cardiac arrest.⁹² Cardiac arrest from myocardial infarction and ischemia can occur from injury to the coronary arteries due to arterial spasm or dissection.⁹² Penetrating trauma to the heart and connecting vessels causes blood to rapidly flow into the pericardial cavity, and is the commonest cause of tamponade, resulting in accumulation of fluid in the pericardial cavity with compression of the heart and decreased cardiac output, eventually resulting in cardiac arrest.⁹⁴

Hypovolemia is usually caused by rapid external or internal blood loss in a trauma patient. Traumatic injury to the limbs may cause estimated blood losses of up to a liter in traumatic fracture of tibia, a maximum of up to 2 liters with fracture of femur and up to 5 liters with traumatic fracture of pelvis.⁹⁵ Compensatory mechanisms include tachycardia, increased cardiac contractility and peripheral vasoconstriction, increased water retention and activation of coagulation cascade.⁹⁵ If hypovolemia is not corrected, hypovolemic shock eventually ensues with multi-organ failure due to decreased cardiac output, metabolic acidosis and organ perfusion that may lead to cardiac arrest.⁹⁵

Cardiac injury because of isolated head trauma is well established and occurs in up to two-third of patients with isolated head trauma.⁹⁶ Isolated head trauma, spinal cord trauma and subarachnoid hemorrhage cause a catecholamine surge that precipitates myocardial injury including necrosis and infarction leading to arrest.⁹⁶ Severe head injury also leads to a phenomenon termed 'impact brain apnea'.^{97,98} Impact brain apnea occurs within the first 10 minutes following traumatic brain injury (TBI) called the critical phase, and is characterized by apnea and massive catecholamine surge.⁹⁶⁻⁹⁸ The apnea and catecholamine release is dependent

on the transmitted force of injury to brainstem.⁹⁶ The combination of hypoxia, hypercarbia and acidosis from apnea and hypertension cause by catecholamines leads to TCA.⁹⁸

Asphyxial cardiac arrest is results from extremely reduced supply of arterial oxygen (hypoxia) and increased arterial carbon dioxide (hypercapnia) due to inability to breathe.^{99,100} The tissue hypoxia and acidosis caused by hypercapnia, have a combined effect on the cardiac conducting system leading to disruptions in rhythm and arrest.¹⁰⁰ Continued asphyxia leads to hypotension and bradycardia that eventually results in arrest, mostly PEA and asystole.¹⁰⁰

In tension pneumothorax, trauma to the chest may cause an opening in the chest wall that forms a one-way valve through which air continues to enter the pleural space but cannot exit. The building air pressure collapses the lung on the injured side, shifts mediastinum and compresses the heart and the vena cava, reducing venous return to the heart and decreasing cardiac output leading to cardiac arrest.¹⁰¹

6.5 CLINICAL PRESENTATION

The clinical manifestations of cardiac arrest in trauma patients varies with the type and mechanism of trauma. It may be difficult to pick up signs of cardiac arrest in a trauma patient. Chest pain and dyspnea, arrhythmias, thrill, rub, murmur, hypotension and tachycardia are characteristic of cardiac injury.^{92,93} The etiology of TCA influences the initial rhythm of the arrest.⁸⁴ Shockable rhythm is common in OHCA with secondary trauma.⁸⁹

Cardiac tamponade in a patient with penetrating or blunt chest trauma may present with tachycardia, tachypnea, drowsiness or unconsciousness, dyspnea, hypotension and distended neck veins.^{94,102,103} Feeble pulse and pulsus paradoxus (decreased systolic blood pressure [SBP] on inspiration), and bradycardia leading to cardiac arrest may occur.¹⁰³

Hypovolemia is quite evident with external hemorrhage, but signs maybe missed with internal bleeding. Signs of hypovolemia include systolic hypotension, tachycardia, tachypnea, decreased pulse pressure, delayed capillary refill, cool clammy skin, low urine output and altered mental status.¹⁰⁴ Symptoms of fatigue, confusion and dizziness should alert to signs of hypovolemic shock.¹⁰⁴ TCA due to hypovolemia usually leads to non-shockable rhythm; PEA (53.1%) and asystole (48.6%).⁸⁴

Severe head trauma/ TBI patients with cardiac injury present with apnea, hypertension or hypotension, decreased consciousness and low Glasgow Coma Scale (GCS) of 3, fixed dilated pupils and absence of pulse.⁹⁶ Severe head injury may lead to cardiac arrest; ventricular fibrillation (50%) in majority of the TCA patients.⁸⁴

Patients with respiratory trauma or respiratory obstruction will have a choking-like state with coughing, gasping and struggling breathing efforts, difficulty to speak, inspiratory stridor, intercostal/subcostal retractions, tachycardia, sweating and confusion/ agitation. Presence of confusion or decreased level of consciousness, weakening respiratory efforts and cyanosis are signs of impending cardiac arrest.¹⁰⁵ Asphyxial cardiac arrest frequently presents with bradycardia and asystole.¹⁰⁶

Tension pneumothorax presents as acute chest pain and shortness of breath, anxiety and fatigue. Signs of tension pneumothorax include deviation of trachea, hyper-expanded chest with increased percussion note, decreased breath sounds and chest expansion, tachycardia and tachypnea, hypotension and hypoxia, hemodynamic collapse and traumatic arrest, often with PEA.¹⁰¹

6.6 EMERGENCY MANAGEMENT

The ‘chain of survival’ remains largely the same for layperson and community actions in TCA, as discussed in Chapter 5.7, with rapid activation of EMS, immediate initiation of CPR and rapid use of automated external defibrillator (AED) as indicated.³ However, the key difference is consideration and urgent management for reversible causes of TCA, that should be considered simultaneously along with and even prioritized over chest compressions in CPR.⁸⁹ The reversible causes of TCA that should be urgently managed include hypoxia, hypovolemia, pneumothorax, pericardial tamponade and hypothermia.¹⁰⁷ The reason for prioritizing immediate management of reversible causes in TCA is that chest compressions are not equally beneficial as in non-TCA, caused by hypovolemia, tension pneumothorax and tamponade.⁸⁹

Essentially BLS and ACLS are the same as for non-traumatic cardiac arrest with some modifications.^{107,108} In a traumatic patient, the cervical spine should be protected.¹⁰⁸ BLS modifications include: for establishing airway, jaw-thrust should be utilized in place of head tilt-chin lift maneuver; rescue breaths should be provided using a barrier or pocket/ bag-mask device to avoid contact with patient’s blood; control of external bleeding by compression bandages and continued standard CPR and defibrillation.^{107,108}

ACLS modifications include the following: consideration of cricothyrotomy if ventilation is inadequate and airway insertion is not possible due to airway trauma; decreased breath sounds on one side with positive-pressure ventilation (PPV) should indicate pneumothorax, hemothorax or diaphragm rupture; treatment of reversible causes; control of external bleeding and replacement of blood loss by fluids to correct hypovolemia; resuscitative thoracotomy should be considered in select patients.¹⁰⁸

Airway placement and ventilation are critical in TCA to reverse hypoxia.⁸⁹ Tracheal intubation is recommended but basic airway support and supraglottic airway should be utilized in case intubation cannot be performed.⁸⁹ Hypotension is further worsened by PPV in hypovolemia and less aggressive respiratory management in such patients is preferred.⁸⁹

External hemorrhage management is life-saving in hypovolemic TCA patients. Pre-hospital hemorrhage control measures include pressure dressings, tourniquets, hemostatic agents, splints, IV fluids, blood products and tranexamic acid (within 1 to 3 hours of trauma).⁸⁹ The principles of damage control resuscitation approach in a hemorrhaging patient includes the following:

- permissive hypotension - IV fluids infusion to achieve pulse and SBP of 80-90 mmHg for maximally 60 minutes.

- hemostatic resuscitation - blood products infusion in recommended equal ratio (1:1:1) of packed red blood cells, platelets and fresh frozen plasma using massive transfusion protocols
- damage control surgery.⁸⁹

Severe head trauma or TBI patients in apnea and without pulse should be ventilated as early as possible for prevention of hypoxia, and rescue breaths along with chest compressions should be provided by bystander till EMS arrive for advanced airway management and ventilation.⁹⁸

For tension pneumothorax, immediate chest decompression with needle thoracostomy should be performed, especially by EMS in prehospital management.¹⁰¹ However, needle thoracostomy has its complications and should only be used when clear signs of tension pneumothorax with hemodynamic collapse are imminent.¹⁰¹ The preferred management of tension pneumothorax is chest tube insertion in the pleura by surgical thoracostomy and has been performed in prehospital phase by physician staffed EMS services.^{89,101,109,110}

In case of cardiac tamponade emergency pericardiocentesis (preferably ultrasound guided) is of benefit and should be performed in pre-hospital phase.^{89,107} However, immediate resuscitative thoracotomy is superior to pericardiocentesis in terms of survival and should be performed as soon as possible.¹⁰⁷

6.7 OUTCOMES

Historically, survival from TCA was very poor.¹¹¹ Prior to 2005, TCA studies reported survival rates from 0% to 3.7% with poor functional outcomes in survivors, and guidelines recommending termination of resuscitation in TCA patients.^{86,111-114}

However, recent studies since then have reported better survival rates in TCA patients ranging from 1.7% to 8%.^{11,82,22,113} Improvements in survival can be attributed to physician staffed EMS systems and aggressive management of TCA patients including prehospital chest decompression and thoracotomy.^{19,113} In 2010 and 2015, guidelines were issued for management of TCA.^{89,108}

Survival also depends on the type and etiology of injury. Cardiac arrest in penetrating injuries have higher survival rates and better neurological outcomes compared to blunt injuries.¹¹²⁻¹¹⁴ However, few studies have reported better outcomes in blunt injuries.^{17,86} TCA patients with isolated head injury have better survival rates.¹¹² In a study by Lockey et al., TCA patients with hypoxemia were reported to have a survival rate of 17%.¹¹³ Hypovolemic TCA patients have poor survival rates. TCA patients in shockable rhythm (VF/pVT) have better survival rates compared to bradycardia and non-shockable rhythms (PEA/asystole).¹¹⁶⁻¹¹⁹

Prehospital times should be as short as possible and rapid transport for surgical intervention with ‘scoop and run’ approach is recommended.^{89,114} Duration of prehospital CPR is indicative of survival in TCA with studies reporting mortality with prehospital CPR and transport time greater than 10 to 15 minutes.¹¹⁴

7 ETHICS

Research in patients with emergency poses a unique challenge. Protecting patients' rights and ethical guidelines require informed consent for all human subject research. However, research in cardiac arrest patients or in prehospital and emergency resuscitation science usually does not allow informed consent to take place because of the patient's emergency condition, patients' loss of consciousness and lack of capacity to give informed consent, time constraints, unsuitable environment, lack of research personnel and immediate patient care requirements.¹²⁰ Considering the above-mentioned difficulties in obtaining informed consent in emergency situations, regulations were issued in 1996 called the 'Final Rule,' that allowed exception to informed consent to conduct essential emergency and resuscitation science research.^{120,121}

The thesis and constituent studies are based on establishment of an out-of-hospital cardiac arrest registry in Qatar. The ethics approval for the registry was sought from the Institutional Review Board (IRB) of Hamad Medical Corporation (HMC), the public healthcare system in Qatar.

As part of the process for ethics approval, ethics documents were requested from the Cardiac Arrest Registry to Enhance Survival (CARES) in United States. CARES registry was formed as a result of collaboration between Emory University and Centers for Disease Control and Prevention (CDC). Documents received from CARES stated that the CDC considers CARES to be a quality improvement intervention and public health surveillance activity.

The Emory University IRB determined that the CARES registry and planned studies were from their viewpoint a quality improvement intervention and public health surveillance activity which is covered by "Privacy Rule" and, therefore did not need any further ethical permits. This answer was given the document number 1377-2004.

The ethics application to the IRB of HMC in Qatar, included a waiver of informed consent form. The HMC IRB determination was similar that the planned research was categorized as public benefit or service programs, and the registry falls under ethics exempt category, the answers were numbered as JIRB# 13-00071.

Study IV also included a sub-study population of in-hospital traumatic cardiac arrest patients which were not mentioned under the inclusion criteria in the JIRB# 13-00071 application. We had to apply for a separate IRB application (JIRB 14384_14) that was also granted approval and similarly classified as JIRB# 13-00071.

8 METHODS

8.1 SETTING – STATE OF QATAR

Qatar is a rapidly developing high-income country and one of the wealthiest in the world.¹²² The country is located in the Arabian Gulf on north eastern part of Arabian Peninsula.¹²³ It shares a land border with Saudi Arabia to the south and nearby countries include Bahrain, United Arab Emirates and Iran.¹²³ Since discovery of oil in the 1940s, and becoming an independent State in 1971, the country has witnessed rapid growth and development.^{123,124} The country has an economy largely based on oil and natural gas reserves.¹²⁴

Qatar's current population as of April 2017, is 2,675,522.¹²⁵ Majority of the population comprised of young working expatriates, with predominantly male (72.6%) population and median age being 32.6 years.^{122,123} The local Qatari's constitute approximately 20% of the total population.¹²⁶ Approximately 45% of the population is comprised of expatriates from the Indian subcontinent.¹²³ Expatriates from other Arab countries account for 20% of the population.¹²³ Expatriates from Philippines also contribute to approximately 10% of the population.¹²³

The birth rate was 11.8 per 1000 people and infant mortality rate was 6.8 per 1000 live births, in 2015.¹²² Life expectancy at birth was 78.8 years.¹²² Qatar has one of the world's lowest death rate at 1.5 per 1000 population.^{122,123}

8.2 HEALTHCARE SYSTEM

The national public healthcare system for secondary and tertiary care is government funded and provided by Hamad Medical Corporation (HMC), in Qatar.¹²⁷ HMC manages one tertiary care general hospital, two community hospitals, seven specialized hospitals, home healthcare services and the national EMS; Hamad Medical Corporation Ambulance Services (HMCAS).¹²⁷ HMC is the first academic health system to have all its hospitals accredited as Academic Medical Center by Joint Commission International.¹²⁷ The graduate medical residency programs at HMC are accredited by the Accreditation Council for Graduate Medical Education International. HMC hospitals are also the teaching hospitals for Weill Cornell Medical College Qatar and Qatar University College of Medicine.¹²⁷

Primary health care corporation provides primary healthcare through its twenty-three primary healthcare centers, all across Qatar.¹²⁸ Of these, thirteen health centers are located in the capital city of Doha while the remaining provide healthcare services to the rest of the country.¹²⁸

The national EMS is structured as a hub and spoke model, with central ambulance centers serving as hubs and spokes representing satellite ambulance units spread all over the country for rapid prehospital care delivery.¹²⁹ There is a central EMS activation number '999'.¹²⁹ The EMS service consists of 1454 personnel, 167 ambulances, 20 rapid response vehicles and helicopter ambulance service.¹²⁹ Qatar's EMS system is three-tiered for emergencies requiring prehospital critical care (e.g. cardiac arrest); ambulance unit, supervisor unit and rapid response unit.¹³⁰

Qatar's EMS geographically disperses ambulances (with 2 ambulance paramedic staff per ambulance) rapid response vehicles (with 1 critical care paramedic and 1 ambulance paramedic), supervisor units (with 1 ambulance paramedic), patient transport units (with transport paramedic staff and ambulance paramedic staff) and helicopters (with 1 critical care paramedic and 1 ambulance paramedic) across the country.

8.3 OUT-OF-HOSPITAL CARDIAC ARREST REGISTRY AND TRAUMA REGISTRY

Registries are important for public health surveillance: disease epidemiology and incidence; reporting outcomes and survival rates; monitoring and identification of high-risk population; comparison and benchmarking of healthcare standards; health disparities and equity; opportunities for community-based prevention programs; identify deficiencies and gaps; ascertain effectiveness and quality of care and more efficient distribution of resources.^{26,131}

There are many OHCA registries including CARES in US, Victorian Ambulance Cardiac Arrest Registry (VACAR) in Australia and Swedish Registry for Cardiopulmonary Resuscitation (SRCR).²³ OHCA registries mostly follow Utstein guidelines for data collection and reporting of OHCA.^{3,23} Utstein-based guidelines included twenty-nine core elements that were considered essential for reporting of OHCA. These variables included date of arrest, discharge/death; birth date/ age; sex; arrest etiology; arrest location; witnessed arrest; chest compressions; bystander CPR; successful bystander CPR; resuscitation attempted or not attempted by EMS; initial recorded rhythm; shockable/nonshockable rhythm; attempted defibrillation; bystander defibrillation; assisted ventilation; prehospital medications; disposition; ROSC; survival and neurological outcome.²¹ This thesis involved establishment of OHCA registry in Qatar, based on Utstein criteria.

The Trauma registry at Hamad General Hospital, the only Level I trauma center in Qatar was established in 2007, according to standards of American College of Surgeons Committee on Trauma.¹⁶ The trauma registry prospectively enrolls all trauma patients that are admitted by the trauma service in Hamad General Hospital.¹⁶ The registry included variables on trauma patient demographics, work-related variables, injury mechanism, risk factors, pre-hospital and EMS care, injury severity scoring (ISS), management, length of stay, complications and survival.¹⁶

8.4 PATIENTS

The patients in the four constituent studies included: OHCA patients in Qatar from June 2012 to May 2013 (Study I); OHCA patients in Qatar from June 2012 to May 2015 (Study II); OHTCA patients in Qatar from January 2010 till December 2015 (Study III); TCA (OHTCA and IHTCA) patients in Qatar from January 2010 till December 2015 (Study IV).

Table 1: Characteristics of study populations

Study	Inclusion criteria	Exclusion criteria
I	Adult, greater than 18 years of age, presumed cardiac origin OHCA patients with EMS-attempted resuscitation, in Qatar	OHCA patients with clear signs of death on EMS arrival
II	Adult, OHCA patients with presumed cardiac etiology and Middle Eastern GCC or North African ethnicity that had EMS-attempted resuscitation, in Qatar	OHCA with clear signs of death on EMS arrival; ethnicity besides Middle Eastern GCC or North Africa; and arrest location during EMS interfacility transfer, nursing home or rehabilitation and long-term health facility.
III	Adult, OHTCA patients that had prehospital cardiac arrest and received prehospital bystander or EMS CPR and had EMS-attempted resuscitation, in Qatar	OHTCA patients with clear signs of death on EMS arrival; OHTCA patients that had burns, submersion and electrocution; TCA (IHTCA) patients that had only in-hospital cardiac arrest and did not receive prehospital bystander or EMS CPR
IV	Adult IHTCA patients that had only in-hospital cardiac arrest in ED or hospital and did not receive prehospital bystander or EMS CPR in Qatar Adult, OHTCA patients that had prehospital cardiac arrest and received prehospital bystander or EMS CPR and had EMS-attempted resuscitation, in Qatar	TCA (OHTCA and IHTCA) patients with obvious signs of death and patients with burns, submersion and electrocution.

8.5 DATA COLLECTION

For establishment of OHCA registry the primary source of data was from Qatar's EMS. The EMS prospectively collects data on all OHCA patients as part of routine clinical care that is stored in the EMS database. The EMS paramedics fill out a prehospital care record that is based on Utstein template for each OHCA patient that is resuscitated by EMS. All EMS prehospital care records were paper based and entered electronically into the EMS database by a dedicated EMS data audit team.

The data variables for OHCA patients are then extracted from the EMS database for the purposes of OHCA registry. The prehospital record and variables of each OHCA patient were linked to the common electronic medical record (EMR) of HMC, the public health system in Qatar. The elements linking prehospital EMS record to hospital EMR include patients name, national identification number, age, sex, medical record number, date of arrest and time of admission to ED. The in-hospital patient medical record file was also retrieved for each OHCA patient that survived to ED admission, for data collection on in-hospital management, hospital course, and follow-up. Since ethics approval did not allow contact with OHCA survivors, follow-up data was obtained by reviewing the medical notes of OHCA patients' successive follow-up visits to the hospital.

For OHTCA study (study III), patients from OHCA registry were linked to the Trauma registry by the same data elements utilized to link prehospital records with EMR. Similar process as for OHCA patients was followed for data collection on OHTCA survivors to ED admission.

For OHTCA and IHTCA study (study IV), IHTCA patients were identified utilizing only the Trauma registry (since OHCA registry identifies only OHTCA patients). All IHTCA patients were survivors to ED admission since they had their first cardiac arrest in ED or in-hospital. Therefore, hospital medical record files were retrieved and data collected on in-hospital variables on all IHTCA patients.

8.6 STUDY DESIGNS AND OUTCOMES

The study designs of the four constituent studies included: observational population-based study (Study I); retrospective cohort study (Study II); observational population-based study (Study III); retrospective cohort study (Study IV).

Table 2: Study design and outcomes of each study

Study	Study Design	Outcomes
I	Observational population-based study on OHCA patients in Qatar	Primary outcome – ROSC and survival to hospital discharge Secondary outcomes – predictors of survival and neurological status at discharge
II	Retrospective cohort study Exposure group: OHCA patients with expatriate/immigrant North African ethnicity in Qatar Comparative group: OHCA patients with local Middle Eastern GCC ethnicity in Qatar	Primary outcome – comparison of covariate variables and survival between North African and Middle Eastern GCC ethnicity Secondary outcome – predictors of ROSC and survival to hospital discharge
III	Observational population-based study on OHTCA patients in Qatar	Primary outcome – survival to hospital discharge Secondary outcome – ROSC
IV	Retrospective cohort study Exposure group: IHTCA patients with cardiac arrest only in ED/in-hospital Comparative group: OHTCA patients with prehospital cardiac arrest	Primary outcome – comparison of covariate variables and survival between OHTCA and IHTCA patients

8.7 STATISTICAL ANALYSIS

The main statistical methods are detailed in the respective studies. Statistical methods are summarized in Table 3.

Table 3: Summary of statistical methods

	Study I	Study II	Study III	Study IV
<u>Comparison between 2 groups:</u>				
Categorical variables:				
Fisher's exact test	X	X	X	
Chi-square test	X	X	X	X
Continuous variables:				
Independent samples T test	X	X	X	X
Mann-Whitney U test	X	X	X	X
<u>Multivariable analysis:</u>				
Logistic regression	X	X	X	X

9 RESULTS

9.1 STUDY I

“Epidemiology and outcomes of out-of-hospital cardiac arrest in Qatar: A nationwide observational study.”¹³⁰

9.1.1 Main findings

Over a one-year period, 447 adult patients with presumed cardiac etiology OHCA in Qatar, were included in the study. (Table 4) The crude incidence and age-sex standardized incidence of EMS-attended OHCA in Qatar, was 23.5 and 87.8 per 100,000 population, respectively. Greater than half of the OHCA were unwitnessed (60%). Approximately 20.6% of OHCA patients received bystander CPR. Initial shockable rhythm was present in 19.7% of the patients. Defibrillation was provided by bystander in 2.7% of OHCA patients and by EMS in 39.2% OHCA patients. ACLS interventions were provided by EMS to 95.3% OHCA patients. EMS time intervals were as follows: median response time was 8.72 min (IQR=6.8–11.8); median scene time was 37.9 min (IQR = 28.0–50.6); median transport time was 21.4 min (IQR = 13.7–31.5). Survival to hospital admission or ROSC was achieved by 58 (13%) OHCA patients and survival to hospital discharge was achieved by 36 (8.1%) OHCA patients. (Table 5 and 6)

Table 4: Common OHCA ethnicities in Qatar

Ethnicity	Number of patients (%)
South Asians (Indian, Nepalese, Pakistani, Bangladeshi, Sri Lankan)	188 (45.3)
Qatari	89 (21.4)
Arabs (other than Qatari)	64 (15.4)
Africans	21 (5.1)
Filipino	20 (4.8)
Caucasians	11 (2.7)

Table 5: Multivariable analysis of predictors of survival to hospital admission

Covariates	Unadjusted odds ratio (95% CI), p-value	Adjusted odds ratio (95% CI), p-value
Respiratory disease	3.34 (1.2–9.2), p = 0.02	8.8 (2.8–27.5), p = 0.001
Shockable initial rhythm	5.44 (3.0–9.8), p = 0.001	4.7 (2.4–9.4), p = < 0.001
Scene time	0.97(0.95–1.0), p= < 0.001	0.98 (0.96–1.0), p = 0.038
Transport time	0.97(0.95–1.0), p = 0.01	0.97 (0.95–1.0), p = 0.02

Table 6: Multivariable analysis of predictors of survival to hospital discharge

Covariates	Unadjusted odds ratio (95% CI), p-value	Adjusted odds ratio (95% CI), p-value
Sex (Male)	0.71 (0.32–1.6), p = 0.4	0.27 (0.1–0.8), p = 0.01
Shockable initial rhythm	11.4 (5.3–24.6), p = < 0.001	13.4 (5.4–33.3), p = < 0.001
EMS ACLS provision	0.11 (0–0.3), p = 0.00	0.15 (0.04–0.5), p = 0.02

9.2 STUDY II

“Ethnic differences in out-of-hospital cardiac arrest resuscitation among Middle Eastern GCC Arabs and North African populations living in Qatar”

9.2.1 Main findings

Over a 3-year period, 397 OHCA patients with Middle Eastern GCC ethnicity (n=285, 71.8%) and North African ethnicity (n=112, 28.2%) were analyzed. In comparison with the local Middle Eastern GCC OHCA patients, the immigrant North African OHCA patients were majority male (p= 0.02), younger (p= 0.001), had greater shockable rhythm (p = 0.01), higher median scene time (p= 0.02) and lesser diabetes (p=0.03). (Table 7)

Table 7: Multivariable analysis of OHCA patients according to Ethnicity

Variable	GCC N =285 (71.8%)	North Africa N= 112(28.2%)	Unadjusted Odds Ratio (95% CI) p-value	Adjusted Odds Ratio (95% CI) p-value
Age (Mean ±SD)	66.9±17	52.3±15	0.95 (0.94-0.96) P=0.001	0.11 (0.04 - 0.29) p= 0.001
Female N (%)	114 (40.0)	17 (15.2)	0.27 (0.15-0.47) P=0.001	0.42 (0.21 - 0.87) p= 0.02
History Diabetes N (%)	118 (44.5)	18 (18.8)	0.29 (0.16-0.51) p=0.001	0.48 (0.25 - 0.91) p=0.03
Shockable Rhythm N (%)	26 (9.3)	23 (21.1)	2.6 (1.41-4.80) p=0.002	2.86 (1.30 - 6.33) p = 0.01
Scene Time (Median, IQR)	37.1 (29.7- 45.0)	43.4 (33.2- 54.6)	1.02 (1.01-1.03) p=0.005	1.02 (1.0 - 1.04) p= 0.02

Survival to hospital admission or ROSC (p=0.92) was achieved by 29 (10.2%) Middle Eastern GCC OHCA patients and 11 (9.9%) immigrant North African OHCA patients. (Table 8)

Table 8: Multivariable analysis of predictors of survival to hospital admission (ROSC) after adjustment for age, gender and ethnicity

Covariates	Unadjusted odds ratio (95% CI), p-value	Adjusted odds ratio (95% CI), p-value
Respiratory Disease	3.35 (1.15-9.8), p=0.03	5.8 (1.7-20.4), p=0.005
Arrest Witnessed	2.13 (1.1-4.2), p=0.03	2.6 (1.1-6.6), p=0.03
Transport Time	0.96 (0.93-0.99), p=0.006	0.94 (0.90-0.99), p=0.009

Survival to hospital discharge (p=0.04) was achieved by 14 (5%) Middle Eastern GCC OHCA patients and 12 (10.7%) immigrant North African OHCA patients. (Table 9).

Table 9: Multivariable analysis of predictors of survival to hospital discharge after adjustment for age, gender and ethnicity

Covariates	Unadjusted odds ratio (95% CI), p-value	Adjusted odds ratio (95% CI), p-value
Diabetes	0.22 (0.06-0.74), p=0.01	0.24 (0.07-0.84), p=0.03
Shockable Rhythm	5.32 (2.16-13.12), p=0.001	4.36 (1.55-12.3), p=0.005
ROSC	8.5 (3.57-20.13), p=0.001	5.02 (1.68-15.02), p=0.004

9.3 STUDY III

“Cardiopulmonary resuscitation of out-of-hospital traumatic cardiac arrest in Qatar: A nationwide population-based study”¹⁵¹

9.3.1 Main findings

Over a 6-year period, 480 patients had OHTCA, in Qatar. After exclusion, 410 OHTCA patients were analyzed. OHTCA in Qatar, had a mean incidence rate of 4 per 100,000 population. OHTCA patients were predominantly male (92.0%) with median age of 33 (IQR 27–46). Blunt injuries (93.4%) caused majority of OHTCA. Road traffic accidents (RTA) were the mechanism of injuries for most of the OHTCA patients. Severe head injury (66.0%) was frequent with most OHTCA patients having mean GCS score of 3 (88.5%). Witnessed OHTCA was 11% and 5% of OHTCA patients received bystander CPR. Initial shockable rhythm was present in 3% of OHTCA patients. Nearly a quarter of the OHTCA patients had cardiac re-arrest.

Prehospital emergency interventions were as follows: 10.2% OHTCA patients were defibrillated; 86% had airway placement; 72.4% were administered IV fluids; 69.8% were given adrenaline; control of hemorrhage was attempted in 10% and needle chest decompression was performed on 3.4% OHTCA patients.

In-hospital emergency management were as follows: 6% of OHTCA patients had thoracotomy; 15% received blood transfusion; 7% had surgery.

Survival to hospital admission or ROSC was achieved by 61 (15%) OHTCA patients. (Table 10) Survival to hospital discharge was achieved by 10 (2.4%) OHTCA patients. The low number of observations for survival did not permit for multivariable analysis. (Table 11)

Table 10: Multivariable analysis of predictors of survival to hospital admission

Covariates	Unadjusted odds ratio (95% CI), p-value	Adjusted odds ratio (95% CI), p-value
Initial shockable rhythm	5.46 (1.65–18.03), p = 0.005	6.39 (1.3–30.7), p = 0.02
Hemorrhage control	3.75 (1.82–7.7), p < 0.000	5.86 (1.9–18.0), p = 0.002
Needle thoracostomy	4.75 (1.6–14.2), p = 0.005	5.28 (1.3–21.7), p = 0.02

Table 11: Univariate analysis for predictors of survival to hospital discharge

Covariates	Unadjusted odds ratio (95% CI), p-value
Initial shockable rhythm	10.12 (0.97–105.23), p = 0.05
Adrenaline	0.045 (0.006–0.358), p = 0.003
Hemorrhage control	4.2 (1.03–16.8), p = 0.045
Blood transfusion	9.22 (2.5–33.7), p = 0.001
Surgery	32.1 (7.54–136.6), p < 0.000

9.4 STUDY IV

“In-hospital traumatic cardiac arrest”

9.4.1 Main findings

Over a 6-year study period, 199 patients had IHTCA in Qatar. IHTCA in Qatar, had a mean incidence rate of 2 per 100,000 population. Majority of IHTCA patients were male (90.4%) with median age 33.5 (IQR 25–48.3). Majority of IHTCA was caused by blunt injuries (96.0%). RTAs were the mechanism of injury for most of IHTCA. Anatomical injuries in IHTCA patients included the following: head injury (60.3%); spinal injury (20.1%); chest injury (22.1%); abdominal injury (35.2%). IHTCA etiology involved hypovolemia in 45.7% patients and hypoxia in 42.4% patients. Mean GCS score was 6.56 ± 4.68 . Initial shockable rhythm was present in 7.5% IHTCA patients. Survival to hospital discharge was achieved in 7.5% of IHTCA patients.

After adjustment for age and gender multivariable analysis showed that IHTCA was associated with spinal injury, abdominal injury, higher prehospital GCS, cardiac re-arrest and survival. (Table 12)

Table 12: Multivariable analysis of comparison between OHTCA and IHTCA patients

Variable	OHTCA N=410	IHTCA N=199	Unadjusted Odds Ratio (95% CI) p-value	Adjusted Odds Ratio (95% CI) p-value
Spinal injury	28 (6.8%)	40 (20.1%)	3.43 (2.04-5.76) p <0.00	3.5 (1.5-8.3) p = 0.004
Abdominal injury	67 (16.3%)	70 (35.2%)	2.78 (1.88-4.11) p <0.00	2.0 (1.0-3.8) p = 0.037
Prehospital GCS (Mean \pm SD)	3.44 \pm 1.9	6.56 \pm 4.68	1.34 (1.25-1.43) p <0.00	1.4 (1.3-1.6) p <0.00
Re-arrest	97 (23.7%)	103 (51.8%)	3.36 (2.3-4.8) p <0.00	5.97 (3.3-10.8) p <0.00
Survival	10 (2.4%)	15 (7.5%)	3.26 (1.4-7.4) p = 0.005	6.3 (1.3- 31.2) p = 0.025

10 DISCUSSION

Globally, OHCA is an important public health problem. It affects millions of people annually and carries high morbidity and mortality.²⁴ With increased trauma burden in developing countries, cardiac arrest of traumatic origin has assumed greater significance, with revised guidelines for aggressive management of TCA.¹⁰⁷

10.1 Are incidence and outcomes of OHCA in Qatar comparable to North America, Europe and Asia?

There is wide variation in reported results of incidence and outcomes in OHCA studies.²⁴ The most recent reported figures of incidence of EMS-assessed OHCA from US and Europe, were 110.8 and 84 per 100 000 population, respectively.^{4,132} In *Study I*, we determined that the age-sex standardized incidence rate of EMS-assessed presumed cardiac etiology OHCA in Qatar was 87.8 per 100,000 population.¹³⁰ The incidence of OHCA in Qatar, closely matches that of Europe.

Survival rates of OHCA have similar variation.²⁴ *Study I* determined Qatar's OHCA survival rate to be 8.1%.¹³⁰ Comparable survival rates in Asia are 5.6% for Japan and 9.9% for Korea, remaining survival rates in Asia were much lower.²⁵ Survival rates for Europe and US were higher comparatively at 10.7% and 12%.^{3,81}

10.2 Is female gender a predictor for higher survival rates in OHCA?

Various studies have reported a gender-specific role in incidence and survival of OHCA.^{29,133,134} The results remain controversial, however. A recent meta-analysis concluded that women with OHCA had better survival compared to males.²⁹ Another study from Resuscitation Outcomes Consortium (ROC) Epistry-Cardiac Arrest registry in North America reported that women with OHCA had a greater likelihood of survival than men in the younger age group of 15 to 45 years, but there was no difference in survival rates between genders in the older age group of > 55 years.¹³³ Similar results were obtained in PAROS study, with women in reproductive age group of 18 to 44 years, having better survival rates compared to men.¹³⁴ The favorable survival rates in younger women could be explained by the cardioprotective role of estrogen in the reproductive age group.¹³³ Findings from *Study I*, show that after adjustment the odds of survival are higher in women with OHCA and are consistent with results from previous studies, however, age stratification was not performed.

10.3 Does bystander CPR improve survival of OHCA in Qatar?

Immediate bystander CPR in witnessed arrest is critical for improved survival and functional status.^{62,63} The bystander CPR rate in *Study I* and *Study II*, was 20.6% and 16.8%, respectively and comparable to bystander CPR rates in Germany (17%) but quite low compared to Netherlands (61%) and Sweden (59%).^{135,136} However, in both *Study I* and *Study II*, bystander CPR had no association with survival.

As soon as a bystander call is received by Qatar EMS, an ambulance is dispatched immediately. The caller is asked further questions and details to confirm OHCA, according to PROQA – priority questions and answers. Telephone-instructions on how to perform CPR are given by EMS dispatcher, once OHCA is confirmed. Dispatcher-assisted CPR has been reported to increase bystander CPR rates and improve survival.⁶³

Further analysis of OHCA patients receiving bystander CPR in *Study I*, showed that 39.4% of bystander witnessed OHCA received bystander CPR. And nearly three-quarters OHCA patients (71%) who received bystander CPR had an initial non-shockable rhythm (PEA or asystole). Only 29% OHCA patients that received bystander CPR had an initial shockable rhythm.

In *Study II*, the effect was even more pronounced. Only 30.5% of bystander witnessed OHCA received bystander CPR. And greater than three-quarters (81%) OHCA patients who received bystander CPR had an initial non-shockable rhythm. Only 19% OHCA patients that received bystander CPR had an initial shockable rhythm.

These results indicate that the community intervention of bystander CPR is lacking in the ‘chain of survival’ for OHCA in Qatar.

- Despite dispatcher-assisted CPR only 39.4% and 30.5% of bystander witnessed OHCA received bystander CPR. Bystanders in majority of the cases do not perform CPR even in witnessed arrest with dispatcher-assisted instructions and guidance on how to perform CPR.
- Approximately three-quarters (71%) or greater (81%) OHCA patients that received bystander CPR were in non-shockable initial rhythm on EMS arrival, indicating late or ineffective CPR.

Studies have shown that barriers to bystander CPR include lack of awareness and training; decreased self-belief in performing CPR; and fear of causing harm, contracting diseases and lawsuit.^{63,137,138} Interestingly, a study from Lebanon reported gender-related barriers to performing bystander CPR that could be applicable to Qatar’s population.¹³⁸ The advent of chest compression-only CPR in absence of the need for rescue breathing will alleviate some of the barriers.^{139,140} Further studies, are required to identify specific barriers to bystander CPR in Qatar.

10.4 Do longer EMS scene times and transport times affect OHCA survival?

The outcomes in OHCA are critically dependent on time to intervention.¹⁴¹ There have been various efforts to decrease the time-interval between cardiac arrest and emergency management.¹⁴² The ‘chain of survival,’ and ‘door to balloon time,’ are emergency processes to reduce time from cardiac arrest to emergency intervention.¹⁴² Prehospital EMS time is subdivided into EMS response time, scene time, and transport time.¹⁴²

Short EMS response times improve OHCA survival rates.¹⁴³ Current recommendations are that EMS response time should be less than 8 minutes.¹⁴³⁻¹⁴⁵ In *Study I* and *Study II*, the median EMS response times were 8.72 and 8.2 minutes, respectively.

However, optimal EMS scene time and transport time for improved OHCA survival are not known.^{146,147} EMS protocols for scene times differ with Asian EMS predominantly adopting a ‘Scoop and run’ model in which OHCA patients are provided resuscitation during rapid transport to the ED with short scene times and limited ALS provision.¹⁴⁶ In contrast, the North American, European and Australian EMS follow the ‘Stay and treat’ model in which EMS staff provide complete ALS interventions till ROSC is achieved or death is declared at scene.¹⁴⁶

A study by Shin et al., demonstrated that survival to admission and good neurological outcome was highest in intermediate scene time (8-15 min), in comparison to short scene time (0-7 min) and long scene time (> 16 min), while survival to hospital discharge was not statistically significant among the groups.¹⁴⁶ Another study by Tijssen et al., exploring scene times in pediatric OHCA survival showed that survival was highest in intermediate scene times of 10 to 35 minutes, compared to the short scene time (< 10 min) and long scene time (> 35 min).¹⁴⁸ In *Study I* the median scene time was 37.9 minutes, while in *Study II*, the median scene time was 39.1 minutes. In *Study I*, increased scene time had an association with decreased ROSC, but there was no effect on survival. In *Study II*, increased scene time was not associated with either ROSC or survival.

Further categorization of scene time in *Study I*, showed that of total 36 OHCA patients that survived to hospital discharge, statistically significant survival was highest in intermediate scene time of 10 to 35 minutes (n=27, 75%), compared to short scene time of less than 10 mins (n=0) and long scene time of greater than 35 mins (n=9, 25%), (p< 0.0001). Our results are consistent with Tijssen et al., that survival was highest in intermediate scene times of 10 to 35 minutes. Interestingly, similar analysis of scene time in *Study II*, did not show an overall statistically significant difference. However, when stratified for ethnicity; Middle Eastern GCC ethnicity had statistically significant survival that was highest in intermediate scene time of 10 to 35 mins compared to short scene time (<10 mins) and long scene time (>35 mins) (p=0.017); North African ethnicity had comparable survival rates in intermediate scene time and long scene time (p=0.671). The migrant North African study population were younger and mostly male and intermediate and longer scene times for ALS provision might have resulted in comparable survival rates compared to the local Middle Eastern GCC study population where intermediate scene times yielded the best results.

EMS transport time should be short to rapidly transport the patient from the scene to ED for coronary intervention and post-resuscitation care. However, longer distances to large health centers with interventional cardiac facilities might result in long transport times.¹⁴⁷ A recent meta-analysis on transport times by Geri et al., included 9 observational retrospective studies and concluded that transport times did not affect survival or neurological function in OHCA.¹⁴⁷ The median transport time in *Study I* and *Study II* was 21.4 minutes and 22.3 minutes, respectively. In both *Study I* and *Study II*, increased transport time had an associated with decreased ROSC, but there was a lack of association with survival.

10.5 Does ethnicity affect OHCA epidemiology, management, health services and survival?

In *Study II*, we showed that compared to the local Middle Eastern GCC OHCA patients in Qatar, the immigrant North African OHCA patients were younger and predominantly male, with lesser risk factors and EMS response time, and greater OHCA outside homes, initial shockable rhythm, ACLS interventions, EMS scene time and survival. Multivariable analysis showed that compared to the local Middle Eastern GCC OHCA patients, the immigrant North African OHCA patients were associated with lesser risk factors (diabetes) and greater initial shockable rhythm and EMS scene time.

Ethnic differences have been reported in incidence, risk factors, witnessed arrest, bystander CPR, initial shockable rhythm, EMS response times and survival rates of OHCA.^{30-33,149,150} African Americans have higher OHCA incidence and risk factors, and lower rates of witnessed arrest, bystander CPR, initial shockable rhythm, and survival. However, Asians and African Americans had shorter EMS response times compared to Caucasians.³³ Generally Caucasians had the best survival rates among African Americans, Asians and Hispanics.^{33,149}

Unlike, previous studies where minorities (e.g. African Americans) have higher risk factors, in *Study II* the minority North African OHCA patients have lesser risk factors. Also, previous studies have shown that minorities (African American) have lower rates of initial shockable rhythm, but the minority North African OHCA patients had greater initial shockable rhythm. Also, previous studies have only looked at EMS response times that were shorter in minorities. In *Study II*, EMS response times were comparable between local and minority groups. However, EMS scene time was greater in the minority North African OHCA patients, indicating greater ALS interventions in this group.

10.6 Chicken or egg: which came first?

Trauma or cardiac arrest: which came first?

TCA is defined as cardiac arrest in a trauma patient.⁸² OHTCA has been defined in prior studies as cardiac arrest occurring in trauma patients during the pre-hospital phase.^{11,82} OHTCA includes primary TCA i.e. trauma causing cardiac arrest and secondary TCA, cardiac arrest leading to secondary trauma.^{89,151,152} In unwitnessed OHTCA patients, there is usually no distinguishing factor to decide which came first: trauma or cardiac arrest? However, cardiac arrest in trauma patients that occurs in ED and during the following hospital course represents only primary TCA. In *Study III* and *Study IV*, we defined 'in-hospital traumatic cardiac arrest,' (IHTCA) as those trauma patients in which cardiac arrest occurs in ED and in-hospital, following a traumatic event and is not cardiac re-arrest. In IHTCA patients, we know that trauma came first.

10.7 Differences in epidemiology, management and outcomes of OHCA in Qatar?

In *Study III*, the mean crude incidence rate of OHTCA in Qatar was determined to be 4 per 100,000 population. In comparison, the crude incidence rate of OHTCA in Melbourne was 6 per 100,000 population.¹¹ OHTCA in Qatar was disproportionately low, since trauma burden of Qatar is nearly three times the burden of trauma in Melbourne.¹⁵³ Bystander witnessed OHTCA and bystander CPR were lower than an Australian OHTCA study, however initial shockable rhythm was higher compared to the same study.⁸⁸ Qatar's majority immigrant (80%), and relatively younger and healthier population could be the explanation for the low numbers of OHTCA despite higher trauma burden, and greater initial shockable rhythm despite lower witnessed OHTCA and bystander CPR.^{11,151,154} Further studies are needed in Qatar, to explore the low incidence of OHTCA in a population with high overall trauma incidence.

Compared to previous studies, *Study III* and *Study IV*, determined that OHTCA in Qatar had the highest reported proportion of blunt injuries in a population-based study. Penetrating injuries caused by gunshot wounds were the second highest cause of OHTCA in a North American study, while there were only 1% OHTCA cases caused by gunshot injuries, in Qatar.⁸² Most penetrating injuries are caused by gunshot, stabbing and assault injuries. And Qatar is one of the safest countries in the world where homicide and assault cases are very few.¹⁵⁵ Hence, penetrating injuries are very low and is the reason for the high proportion of OHTCA caused by blunt injuries.

A study by Chiang et al., reported that prehospital Adrenaline administration in OHTCA patients is associated with improved ROSC and survival rates. However, in *Study III*, we got the opposite result; Adrenaline administration was associated with lower odds of ROSC and survival. The result is explained by Adrenaline having a worsening impact in OHTCA patients with severe head injury (66%) which involves pre-existing pathophysiological catecholamine release.

In *Study III*, prehospital thoracostomy and hemorrhage control were associated with improved ROSC. Although blood transfusion and surgery improved survival, ED/trauma room

thoracotomy was not associated with survival. Previous studies have recommended that thoracotomy is beneficial in mostly penetrating injuries and even that blunt injuries are a contraindication for thoracotomy.^{156,157} Since greater than 90% of Qatar's OHTCA patients have blunt injuries, it is not surprising that thoracotomy was not associated with survival.

ROSC and survival were lower than most recent studies, although Qatar's OHTCA survival rate of 2.4% was higher than the 1.7% survival reported in a recent Australian study.¹¹ However, recent OHTCA studies reported a survival rate of 6-7.5%.^{12,82} The plausible reasons for low OHTCA survival rate in *Study III* and *Study IV* included: inclusion criteria was stricter than previous studies; IHTCA patients were excluded; greater proportion of primary OHTCA patients; greater proportion of blunt injuries causing OHTCA.

10.8 IHTCA: a new study population of TCA and how it differs from OHTCA?

In *Study IV* and *Study III*, we identified a new sub-study population of TCA, and termed it as 'in-hospital-traumatic cardiac arrest,' (IHTCA). IHTCA was defined as cardiac arrest that occurred in ED or in-hospital in a trauma patient and was not cardiac re-arrest.

IHTCA differed significantly from OHTCA in terms of epidemiology, etiology, pathophysiology and survival. In *Study IV*, the incidence of IHTCA was 2 per 100,000 population, approximately half that of OHTCA. In comparison, IHTCA patients: had greater Far Eastern ethnicity; had higher proportion of falls; greater anatomical localization (spine, chest and abdomen); greater hypovolemic etiology; higher mean GCS score; greater initial shockable rhythm and cardiac re-arrest; improved survival to hospital discharge. Multivariable logistic regression analysis showed that IHTCA was associated with spinal injury, abdominal injury, higher prehospital GCS score, cardiac re-arrest and improved survival.

The pathophysiology of IHTCA involves delayed cardiac arrest following trauma. In *Study IV*, we did not place any time-limit in IHTCA patients for cardiac arrest occurrence in-hospital. The reason for this was that the 199 IHTCA patients in *Study IV*, were insufficient to achieve time-based results. Further exploratory prospective study on IHTCA patients is planned to determine a time-period based cut-off for occurrence of cardiac arrest in-hospital that is caused by the traumatic injury.

The anatomical injuries reported in previous OHTCA and TCA studies include head, neck and chest, pelvis and limbs.^{90,91} In multivariable analysis of *Study IV*, IHTCA patients had localization of injury to spine and abdomen, anatomical regions usually not associated with TCA in previous studies. Greater abdominal and spinal injuries in IHTCA patients may represent different pathophysiological mechanisms, for example involving the thoracoabdominal autonomic nervous system, leading to cardiac arrest.¹⁵⁸

In *Study IV*, after adjusting for age and gender; the higher mean prehospital GCS score in IHTCA patients indicate that the trauma in these patients is not as severe, in comparison to

OHTCA patients. IHTCA patients should be aggressively managed, especially since it is associated with improved survival. IHTCA patients had 6.3 odds of survival compared to OHTCA patients. The survival rate of 7.5% in IHTCA patients in *Study IV*, is comparable to the 8.1% survival rate of OHCA patients in *Study I*. IHTCA patients should be aggressively managed since their survival rates are nearly the same as for medical cardiac arrest.

11 CONCLUSIONS

The incidence and survival of OHCA in Qatar, was comparable to results reported from Europe and Asia.

Qatar's EMS response times of 8 minutes are according to recommended guidelines. EMS intermediate scene time interval of 10 to 35 minutes had the best survival rates. EMS transport times are longer, and lowered odds of ROSC but had no association with survival.

Bystander CPR had no association with survival. Community-based public awareness campaigns and chest-compression only CPR training programs would improve bystander CPR and survival rates.

The migrant North African OHCA patients in Qatar were younger and healthier, and had greater shockable rhythm, received greater ALS interventions and had better survival rates compared to the local Middle Eastern GCC OHCA patients.

TCA was redefined to consist of OHTCA and IHTCA. OHTCA incidence and survival rates were lower compared to studies from Europe, North America and Australia. Qatar's OHTCA patients had the highest proportion of blunt injuries reported. Except for thoracotomy, other emergency management interventions; bleeding control, thoracostomy, blood transfusion and surgery, were associated with improved ROSC and survival.

IHTCA differed from OHTCA in terms of lower incidence, pathophysiology of delayed cardiac arrest, anatomical localization of trauma to spine and abdomen, higher mean prehospital GCS score, greater initial shockable rhythm, cardiac re-arrest and improved survival. Aggressive management of IHTCA is recommended since survival rates are approximately equal to OHCA.

12 ACKNOWLEDGEMENTS

I would like to convey my heartfelt gratitude to my family, colleagues, friends and teachers without whom my doctoral thesis would not be possible.

HMC provided me with the support and environment to start, carry out and complete my PhD. There have been contributions from all the colleagues and friends in the departments of Emergency Medicine, Ambulance Services, Cardiology, Neuroscience, Trauma, Medical Research Center and Academic Health System at HMC. HMC is a great place to work and grow, and I look forward to contributing to the advancement of health, education and research in HMC and Qatar.

Peter Cameron is my co-supervisor and the person without whom I would have never been able to start my PhD and advance my career in HMC. I will always remember him fondly as our 'Nana,' the title of maternal grandfather that we gave him out of respect and affection.

Therese Djarv my main supervisor and friend who has supported and guided me throughout my PhD. Her faith and belief in me gave encouragement to reach greater heights and without her I would never have been able to complete my PhD.

Maaret Castren my co-supervisor and first teacher at Karolinska Institute. She was integral in starting my PhD. She is a great person and it has been an honor to be her PhD student.

Stephen Thomas has been instrumental for my PhD and career. Without his support, I would never have been able to complete my PhD. I could not have wished for a better Chair of Dept.

Ashfaq Shuaib has always provided support and guidance for my PhD and career. His advice has been most beneficial and he occupies a very special place as fatherly figure.

Ibrahim Janahi as Executive Director of Medical Research Center, HMC, has provided the support without which my PhD could have never happened. Not only with my PhD but he also allowed me to grow and establish the Research Forum and Research Support System, at HMC.

Jassim Al-Suwaidi has also been a great pillar of support and encouragement for my PhD. He always urged me to write bigger and better studies and we have had many good discussions on cardiovascular research.

Rajvir Singh who has been my statistics teacher, colleague and friend. He is one of the best persons I have come across and without him my statistical skills would never be as good.

Rafael Consunji has been a good friend and colleague. His generosity and sharing of data and team work allowed me to work on TCA studies.

Guillaume Alinier is a good friend and colleague. His contribution towards the timely sharing of data and overall team work contributed greatly to all PhD studies.

Sameer Pathan my friend, colleague and fellow PhD student. We both started our doctoral studies together and over the years we have grown and learnt together. I hold him in great esteem.

Zain Bhutta my friend, team member and colleague. Without his help, my PhD would not be possible. He will soon be starting his PhD and I wish him all the best for his doctoral studies.

Pooja George my friend, team member and colleague. Without her help, my PhD studies would not be possible. She started her research with me and I hope she becomes a good physician researcher.

My parents; Irfan Uddin and Farzana Irfan who have spent their lives raising me and my siblings and doing their best to get us where we are all today. I love you both and my achievements would never have been possible without you. You both have been the constant in my life and I am thankful that I am your son.

My brother Affan B. Irfan and sister-in-law Sommaya Naveed, and my sister Bismah B. Irfan and brother-in-law Umair Ashraf. I love you all, especially the babies Aiza and Enaara. Thank you Affan and Bismah for being there always for me. I have been blessed to have you both as my siblings.

My father and mother-in-law: Aziz Tariq Farooqi and Nazli Tariq who have treated and cared for me as their son. I love you both and thank you for giving me your daughter and making me part of your family.

My sister-in-law Yusra Tariq and brother-in-law Syed Anas Mobeen. I love you both and the babies Murtaza and Ayra. Thank you for considering me as your brother.

My wife Tooba Tariq who is wonderful in every way and ensured that I complete my PhD before time. Your love knows no bounds and you are the driver for my success. Love you.

This work was supported by a grant (IRGC-RF-047) from Medical Research Center, Hamad Medical Corporation.

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