

Coronary artery bypass surgery in Syrian refugees

Outcomes in a Turkish tertiary center

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ABSTRACT

الأهداف: لتقييم نتائج اللاجئين السوريين الذين يخضعون لجراحة الشريان التاجي في مستشفى ثالث في تركيا.

الطريقة: بحثنا بالوفيات في المستشفى وجميع مسببات الوفاة لعام 427 كنتائج رئيسية. قمنا بمراجعة سجلات 67 مريضاً سورياً و 427 مريضاً تركياً خضعوا لجراحة تغيير شرايين القلب التاجية المعزولة بين يناير 2015م ويناير 2017م بأثر رجعي.

النتائج: كان كلاً من تاريخ أمراض الشرايين التاجية، وأمراض الشريان السباتي، والسمنة منتشرة لدى المرضى السوريين. كانت مستويات بروتين سي التفاعلي أعلى في المرضى السوريين في حين كانت مستويات الشحوم والوظائف الانقباضية للمجموعتين متشابهة. المرضى السوريين أكثر إصابة بمتلازمة الشريان التاجي الحادة (26.9% مقابل 15.5%، $P > 0.001$). كان SYNTAX I (التأزر بين PCI مع Taxus وجراحة القلب) و SYNTAX II-PCI أعلى في المرضى السوريين في حين كان SYNTAX II-CABG مماثلة مع المرضى الأتراك. كان زمن الأنبوب أطول، وكان مقدار النزف أكبر في المرضى السوريين، ومع ذلك، لم يزداد التنقيح. وبالرغم من أن عدوى الجرح كانت أكثر انتشاراً لدى المرضى السوريين، كانت المضاعفات التالية للجراحة متشابهة بين المجموعتين. لم يظهر اختلاف في معدل الوفيات داخل المستشفى ومعدل الوفاة لكل سنة بين المرضى السوريين والأتراك [1 (1.5%) مقابل 13 (13.1%)، $p=0.476$ ؛ المرضى الأتراك 3 (4.5%) مقابل 25 (5.9%)، $p=0.63$].

الخاتمة: كان لدى المرضى السوريين نتائج أعلى SYNTAX I و SYNTAX II PCI، بينما نتيجة SYNTAX II CABG عالية بالمقارنة مع المرضى الأتراك. كانت المضاعفات أثناء العملية وبعد العملية الجراحية مماثلة. كان معدل الوفيات داخل المستشفى وسنة كاملة من الوفيات لدى المرضى السوريين متشابهين مع المرضى الأتراك. النتائج الجراحية للمرضى السوريين مقبولة. يجب توفير الوقاية الأولية من السمنة. يجب اتخاذ تدابير وقائية ثانوية صارمة بسبب شدة زيادة مرض الشريان التاجي.

Objectives: To assess outcomes of Syrian refugees undergoing coronary artery bypass surgery in a tertiary hospital in Turkey.

Methods: We sought for in-hospital mortality and one year all-cause mortality as the main outcomes. We reviewed records of 67 Syrian and 427 Turkish patients undergoing isolated coronary bypass surgery between 2015 January and 2017 January retrospectively.

Results: History of coronary, peripheral and carotid artery diseases and obesity were more frequent in Syrian patients. C-reactive protein levels were higher in Syrian patients whereas lipid profiles and systolic functions of the 2 groups were similar. Syrian patients more frequently presented with the acute coronary syndrome (26.9% versus 15.5%, $p < 0.001$). SYNTAX I (Synergy between PCI with Taxus and Cardiac Surgery) and SYNTAX II-PCI were higher in Syrian patients whereas SYNTAX II-CABG was similar with Turkish patients. Extubation time was longer and amount of the hemorrhage was greater in Syrian patients; however, bleeding revision was not increased. Although wound infection was more frequent in Syrian patients, postoperative complications were similar between groups. In-hospital mortality and one year all-cause mortality did not differ between Syrian ($n=1$; 1.5% versus $n=13$; 13.1%) ($p=0.476$) and Turkish patients ($n=3$; 4.5% versus $n=25$; 5.9%) ($p=0.63$).

Conclusion: Syrian patients had higher SYNTAX I and SYNTAX II PCI scores, but not SYNTAX II CABG score compared with Turkish patients. Intraoperative and postoperative complications were similar. In-hospital mortality and one year all-cause mortality of Syrian patients were similar with Turkish patients. Surgical outcomes of Syrian patients were acceptable. Primary prevention of obesity must be provided. Aggressive secondary preventive measures must be taken due to increased severity of coronary artery disease.

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Conflict in Syria since 2011 caused a massive refugee displacement. More than 5 million refugees live outside Syria.¹ This is the biggest immigration after World War.² Turkey has accepted the vast majority of refugees. By the date of 22 February 2018, formally reported number of Syrian refugees (SR) under temporary protection of Turkey is 3.554.072.² Istanbul hosts more than half million SR. The success of Turkey in providing healthcare to a large population of refugees was confirmed and reported by international delegations.³ A significant number of papers were published reporting about the health status of SR in Turkey, Jordan, and Palestine.⁴⁻⁶ Trauma-related surgical problems, acute infectious disease and psychiatric disorders are the most common presentations of SR.⁷ Beyond aforementioned diseases related with war and migration, cardiovascular disease was the leading cause of death in Syria before the civil war.⁸ Only a few papers focused on cardiovascular disease in SR, which deserves more attention.^{9,10} Single paper exists which evaluated outcomes of SR undergoing coronary bypass surgery.¹¹ Given the value of this early report, it only presents Syrian patients' records and it lacks comparison with Turkish patients. Furthermore, the study was performed in a Turkey's border city, where SR mostly stayed in camps. Therefore, it was not possible to obtain follow up outcomes. Since Istanbul is a final destination where most SR settle down; thus, we were able to estimate mortality rates in our study.

It is evident that SR tend to be under diagnosed and under treated during years of war. We investigated outcomes of SR undergoing coronary artery bypass (CABG) surgery and compared outcomes with Turkish patients. We sought whether SR have different complication and mortality rates.

Methods. In this retrospective cohort, we sought for in-hospital mortality and one year all-cause mortality as main outcomes. Additionally, preoperative risk factors, operative and postoperative complications were also evaluated. We reviewed records of 511 patients between 2015 January and 2017 January undergoing isolated coronary bypass surgery in Haseki Training and Research Hospital, a tertiary center in Istanbul. We excluded 12 urgent surgeries and 16 cases who had a diagnosis of malignancy. Patients who underwent

off-pump surgery were included in the study (n=28). Eventually, 426 Turkish and 67 Syrian patients were included in the study.

Routine preoperative examinations were performed in all patients. Electrocardiography, echocardiography, carotid Doppler ultrasound and respiratory function tests were performed. Carotid artery angiography was performed in case Doppler ultrasound revealed stenosis above 50%. Twenty-four patients who had carotid artery stenosis underwent carotid endarterectomy (CEA), according to European Society for Vascular Surgery guidelines, at the time of CABG.

The median sternotomy was performed in all cases. Left internal thoracic artery (LITA) and saphenous venous grafts were harvested. Left internal thoracic artery was used for left anterior descending artery where possible. Cardiopulmonary bypass (CPB) was performed via right atrial and aortic cannulation, the aorta was cross-clamped after cooling to 28-32°C. During CPB, mean arterial pressure was maintained at 50-70 mm Hg. Myocardial protection was achieved with continuous retrograde blood cardioplegia whereas anterograde blood cardioplegia was performed at 20-minute intervals. During coronary bypass grafting, proximal anastomoses were performed under side clamp. Anterograde cardioplegia was delivered in the cases only with short estimated operation period. Proximal anastomoses were made under cross clamping in patients with aortic calcifications. Temporary pacemaker was placed in patients suffering from arrhythmia. Coronary bypass was terminated after warming. Sternum was closed when hemostasis was achieved.

Patients were routinely followed up by cardiovascular surgeon and cardiologist on the first week and fourth week of discharge. After the first-month, cardiologist examined the patients at 3-month intervals. Mortality data mostly depends on regular examinations recorded in hospital software data. Additionally, searches were conducted from national death reporting system (<https://obs.gov.tr>). Phone calls with patients or relatives were performed when needed. The study was approved by the local ethical committee.

Statistical analysis. Statistical Analysis for Social Sciences for Windows, Version 17.0. (Chicago: SPSS Inc.) was used for statistical analysis. The normality of the data was tested with Kolmogorov-Smirnov test. Mean ± standard deviation (SD), median and interquartile range (IQR) were used for normally and non-normally distributed variables. Percentages were used for categorical data. Differences in categorical variables between groups were assessed with Chi-square test. Mann-Whitney U or Student's T-test were used to

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assess differences between patient subgroups. P-value <0.05 was considered statistically significant. Survival was examined by Kaplan-Meier analysis between groups. The log-rank test was used to compare survival estimates.

Results. Baseline characteristics. In this retrospective cohort, we sought for in-hospital mortality and one year all-cause mortality as main outcomes. Additionally, preoperative risk factors, operative, and postoperative complications were also evaluated. The study included 426 Turkish and 67 Syrian patients were included in the study. Baseline characteristics of groups are presented in Table 1. Turkish patients were older. Both groups of patients were overweighted; however, BMI is significantly higher in Syrian patients (29.9±3.6 versus 27.1±3.8; $p<0.001$). Obesity (BMI ≥ 30) was more frequent in Syrian (43.3% versus 20.7%, $p<0.001$). Smoking and hypertension were more frequent in Turkish patients. The previous history of coronary artery disease was more frequent in Syrian patients. Although peripheral and carotid artery disease were more frequent in Syrian patients, the severity of carotid artery stenosis did not differ. Both patient groups have similar lipid profiles; however, Syrian patients have significantly higher CRP. Syrian patients were more frequently presented with the acute coronary syndrome (26.9% versus 15.5%, $p<0.001$). Systolic functions of the 2 groups were similar. History of coronary artery disease is more frequent in Syrian. SYNTAX I and SYNTAX II PCI were higher in Syrian patients whereas SYNTAX II CABG was similar compared with Turkish.

Operative and postoperative characteristics. The rate of off-pump surgery and number of grafts implanted were similar between groups (Table 2). Cardiopulmonary bypass time, aortic clamp time did not differ between groups. Intraaortic balloon pump use was similar between groups. Extubation time was longer in Syrian patients [9 (6-10) versus 7 (5-9.5), $p<0.001$] (Table 3). Amount of hemorrhage was greater in Syrian; however, need for bleeding revision were similar between groups. Although sternal wound infection was more frequent in Syrian patients, sternal dehiscence and mediastinitis did not differ. Intensive care unit and clinic stay were not different between groups. In hospital atrial fibrillation, acute renal failure and postoperative stroke were similar between groups. In-hospital mortality was similar between groups. One year all-cause mortality did not differ between Syrian and Turkish patients (n=3 (4.5%) versus n=25 (5.9%), $p=0.63$) (Figure 1).

Table 1 - Baseline characteristics of Syrian and Turkish patients.

Baseline characteristics	Syrian (n=67)	Turkish (n=426)	P-value
Gender (Male/Female)	54/13	342/84	0.952
Age (years)	52.6 ± 8.6	59.9 ± 7.5	<0.001
Body mass index (kg/m ²)	29.9 ± 3.6	27.1 ± 3.8	<0.001
Risk factors			
Smoking	15 (22.4)	178 (41.8)	0.002
DM	22 (32.8)	148 (34.7)	0.761
HT	24 (35.8)	183 (43.0)	0.27
COPD	9 (13.4)	69 (16.2)	0.565
PAD	13 (19.4)	46 (10.8)	0.044
CAD	23 (34.3)	51 (11.9)	<0.001
Stroke	2 (3.0)	22 (5.2)	0.35
Laboratory (mg/dl)			
Total cholesterol	279.4 ± 89.6	267.7 ± 91.7	0.331
LDL	142.7 ± 36.2	134.2 ± 37.3	0.081
HDL	46.1 ± 6.2	45.7 ± 5.7	0.594
CRP	10.0 ± 3.2	6.7 ± 3.4	<0.001
Carotid artery stenosis	17(25.4)	51 (12.0)	0.003
Carotid artery stenosis severity (%)	52.9 ± 16.2	66.0 ± 22.5	0.068
Ejection Fraction (%)	49.4 ± 9.2	50.6 ± 9.1	0.308
CEA	2 (3.0)	22 (5.2)	0.442
Preop MI	18 (26.9)	66 (15.5)	<0.001
SYNTAX I	35.8 ± 8.9	18.2 ± 6.5	<0.001
SYNTAX II PCI	44.2 ± 9.0	34.0 ± 6.7	<0.001
SYNTAX II CABG	27.2 ± 10.6	26.4 ± 7.7	0.417

DM - diabetes mellitus, HT - hypertension, COPD - chronic obstructive pulmonary disease, PAD - peripheral artery disease; CAD - coronary artery disease, CEA - carotid endarterectomy, preop MI - preoperative myocardial infarction

Table 2 - Operative characteristics of Syrian and Turkish patients.

Characteristics	Syrian (n=67)	Turkish (n=426)	P-value
Off pump surgery (%)	4 (6.0)	24 (5.6)	0.912
CPB time (min)	83.0 ± 37.5	77.6 ± 26.7	0.164
Clamp time (min)	44.9 ± 22.4	42.8 ± 15.7	0.353
By-pass graft number	2.7 ± 1.0	2.8 ± 1.0	0.426

CPB - cardiopulmonary bypass

Discussion. Our study showed that Syrian patients undergoing CABG surgery are approximately a decade younger. Obesity seems to be an important comorbidity in Syrian patients. Although coronary artery risk factors are similar with Turkish patients, history of coronary artery disease is more frequent in Syrian patients. Additionally, Syrian patients more frequently presented with the acute coronary syndrome. Syrian patients have more complex coronary artery disease. Higher SYNTAX II PCI score in Syrian patients is more related to coronary complexity rather than clinical risk factors.

Compatible with SYNTAX II CABG score, in-hospital and one year mortality of Syrian patients is similar with Turkish patients. SYNTAX II CABG score predicts outcomes properly in Syrian patients. Longer extubation period may be related with ethnical differences in the metabolization of anesthetics.

Smoking prevalence was about 22% in our study. Depending on the survey of Turkish ministry of health which included 5760 refugees, prevalence of smoking is about 34% among SR.⁶ Some patients may hide

smoking and other habits since they think it may have negative impact on their treatment.

Average BMI was reported as 27.3 and obesity was predicted as 27.7% in the aforementioned survey.¹² Our results are far greater than the survey predicted, which points out the importance of obesity as a significant risk factor for coronary artery disease in refugees. According to the survey, low level of physical activity prevalence is 67% in SR, which increased to 72% between ages of 45 and 59. Cultural food tradition, unsuitable lifestyle and low socioeconomic status are some reasons of obesity.

Posttraumatic stress disorder (PTSD) is more prevalent in SR with a rate of 83.4%.¹³ Relationship between PTSD and coronary artery disease is well established.¹⁴ Although controversy exists, elevated CRP levels may be associated with psychological stress.¹⁵ On the other hand, higher incidence of acute coronary syndromes in SR may be related with higher CRP levels.

Higher prevalence of wound infection may be related to poor hygiene conditions. Besides, compatible with previous studies frequent lower extremity peripheral artery disease might be related to wound infections in Syrian patients.¹⁶ Approximately greater than 100 ml of hemorrhage occurred in Syrian patients. Syrian patients have increased the frequency of acute coronary syndrome, thus excess hemorrhage may be related with dual antiplatelet use. Nevertheless, excess hemorrhage did not result in an excessive surgical revision.

History of cardiovascular disease was reported as 6.4% in the survey of the Ministry of Health.⁶ However,

Table 3 - Postoperative characteristics of Syrian and Turkish patients.

Variables	Syrian (n=67)	Turkish (n=426)	P-value
IABP (%)	5 (7.5)	12 (2.8)	0.053
Extubation time (hours)	9 (6-10)*	7 (5-9.5)	<0.001
Bleeding revision (%)	3 (4.5)	22 (5.2)	0.812
Hemorrhage (ml) (mean±SD)	582.1±183.3	487.9±234.9	0.002
Sternal dehiscence	6 (9.0)	19 (4.5)	0.120
Wound infection	8 (11.9)	19 (4.5)	0.012
Mediastinitis	0	12 (2.8)	0.165
ARF	3 (4.5)	12 (2.8)	0.463
Stroke	0	4 (0.9)	0.427
MI	3 (4.5)	5 (1.2)	0.78
Atrial fibrillation	10 (16.4)	42 (10.4)	0.161
ICU stay (day)	2.7 ± 3.8	2.3 ± 1.6	0.137
Clinic stay (day)	4 (4-5)*	5 (5-6)	0.101
In-hospital mortality	1 (1.5)	13 (3.1)	0.476
One-year mortality	3 (4.5)	25 (5.9)	0.63

** median and interquartile range (IQR), IABP - intraaortic balloon pump, ARF - acute renal failure, MI - myocardial infarction, ICU - intensive care unit

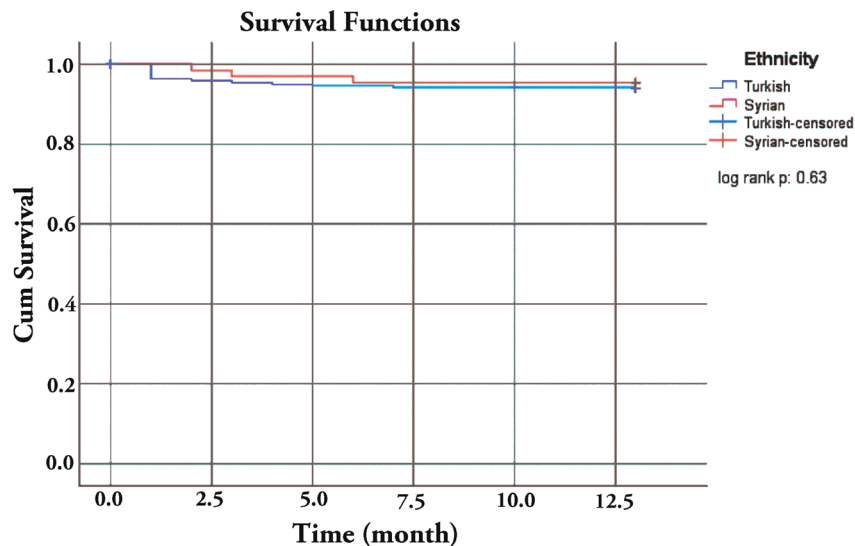


Figure 1 - Kaplan-Meier cumulative survival curves for 1-year mortality according to ethnicity

history of coronary artery disease in our study is 34.3%. Moreover, Syrian patients were more frequently admitted to hospital with the diagnosis of acute coronary syndrome. Compatible with these findings, increased SYNTAX I score in Syrian patients exposed more severe coronary artery disease. Our hospital is a tertiary center; therefore, this may cause an increased cumulative incidence of patients with history of CAD.

High SYNTAX II PCI score seems to be related with SYNTAX I score. SYNTAX II CABG score takes COPD and age more into account which poses a greater risk for CABG, but not for PCI. Similar frequencies of COPD in Syrian and Turkish patients in addition to younger Syrian patients result in similar scores of SYNTAX II CABG. Another reason for severe CAD in Syrian patients may be selection bias of patients between surgery and percutaneous treatment. Although we have not investigated thoroughly, refugees may prefer surgery over PCI, since surgery imposes a significant social, mental and economic burden. Thus, patients with more complex anatomies might have been referred for surgery. Nevertheless, SYNTAX II CABG score is compatible with our in-hospital and one year outcomes.

Restam et al¹⁷ reported increased mortality in coronary heart disease about 60% in Syria between 1996 and 2006. More than two-third of the increase was associated with increased risk factors such as hypertension and cholesterol. Authors emphasized the unhealthy life style due to urbanization and modernization of Arab societies. A cross-sectional survey reported annual cardiovascular crude death as 314 per 100,000 and cardiovascular deaths were responsible for 45% of overall mortality in 2007.⁸ Even before several years of conflict, cardiovascular mortality was worse in Syria compared with Turkey.¹⁸ A systematic literature review concluded that humanitarian emergencies are associated with increased cardiac morbidity and mortality persist for years.¹⁹ According to The Institute for Health Metrics and Evaluation (IHME) at the University of Washington, ischemic heart disease is the second cause of death after conflict and terror in Syria in 2016.²⁰ Furthermore death due to ischemic heart disease increased 14.6% between 2005-2016.

Several studies showed the increased incidence of coronary heart disease in immigrants compared with natural born citizens.²¹⁻²³ Beyond genetic factors, socioeconomic status play role in worse cardiovascular outcomes. However, Hedlund et al²⁴ showed increased acute myocardial infarction incidence in the early years after immigration independent of socioeconomic

status. This early increase may be related to increased psychological stress. Although not assessed in our study, we observe significantly increased psychological stress in Syrian patients whose contribution to disease progression may not be underestimated. In addition to thorough clinical and surgical data, we presented risk scores taking angiographic features into account. Not only nationwide but also international multicenter collaborative studies are required in order to set policies and improve the cardiovascular status of SR.

Study limitations. Retrospective nature of the study is the major limitation. Some deaths were only confirmed from death reporting system which does not present cause of death in details. Although cardiovascular causes comprise greater than 90% of mortality, we found appropriate to present one year all-cause mortality in this study.

In conclusion, Syrian patients had more complex coronary artery disease and higher SYNTAX I and SYNTAX II PCI scores, but not SYNTAX II CABG score compared with Turkish patients. Intraoperative and postoperative complications were similar. In-hospital mortality and one year all-cause mortality of Syrian patients were similar with Turkish patients. Surgical outcomes of Syrian patients were acceptable. Primary prevention, particularly for obesity, must be provided. Aggressive secondary preventive measures must be taken due to increased severity of coronary artery disease.

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