Original Article

Outcome of transcatheter aortic valve replacement in Israeli Jews and Arabs

Hussein Sliman[1], Amnon Eitan[1], Avinoam Shiran[1], Barak Zafrir[1], Basheer Karkabai[1], Moshe Y. Flugelman[1], Naama Schwartz[2,3], Ronen Jaffe[1]

[1]Department of Cardiology, Carmel Medical Center, Haifa, Israel; [2]Research Authority, Carmel Medical Center, Haifa, Israel; [3]School of Public Health, University of Haifa, Haifa, Israel

Contributions: (I) Conception and design: H Sliman, R Jaffe, MY Flugelman; (II) Administrative support: H Sliman, R Jaffe, MY Flugelman; (III) Provision of study materials or patients: B Zafrir, A Eitan, A Shiran, B Karkabai; (IV) Collection and assembly of data: B Zafrir, A Eitan, A Shiran, B Karkabai; (V) Data analysis and interpretation: N Schwartz, H Sliman; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Hussein Sliman, MD. Department of Cardiology, Carmel Medical Center, 7 Michal St., Haifa 3436200, Israel.
Email: dr.hussein.sliman@gmail.com.

Background: Ethnic minorities may face disparities in access to health care and clinical outcomes. Transcatheter aortic valve replacement (TAVR) has an established role in treatment of patients with severe symptomatic aortic stenosis, however outcome of these procedures among different demographics within the multi-ethnic Israeli society is unknown. We sought to compare mortality following TAVR between Jewish and Arab patients in Israel.

Methods: A prospective single-center TAVR registry in northern Israel was analyzed. We compared post-procedural survival among Arab and Jewish patients who underwent TAVR, presenting the estimated hazard ratio (HR) using Cox regression.

Results: Of 923 subjects who underwent TAVR between 2010–2021, 172 (19%) were Arab and 751 (81%) were Jewish. The Arab patient population was younger (mean 77 *vs.* 81 years, P<0.001), had lower prevalence of coronary artery disease (34%, *vs.* 43%, P=0.02), hypertension (80% *vs.* 88%, P<0.01) and calculated procedural mortality (EuroScore II: mean 4.6 *vs.* 4.9, P=0.02), and higher percentage of females (65% *vs.* 53%, P=0.01), body mass index (mean 30 *vs.* 28, P<0.001) and creatinine clearance (mean 67 *vs.* 59 mL/min, P<0.001). Arab patients had similar post-procedural mortality compared to Jewish patients [7-day mortality: adjusted HR 1.51, 95% confidence interval (CI): 0.39–5.77, P=0.55; 30-day mortality: adjusted HR 1.79, 95% CI: 0.62–5.18, P=0.29; 1-year mortality: adjusted HR 1.24, 95% CI: 0.72–2.12, P=0.43].

Conclusions: Arab patients undergoing TAVR were younger and had lower predicted mortality than Jewish counterparts, however, these characteristics did not translate into improved post-procedural survival.

Keywords: Aortic stenosis; transcatheter aortic-valve implantation; ethnicity; Arabs; Jews

Submitted Sep 04, 2023. Accepted for publication Nov 24, 2023. Published online Jan 04, 2024.
doi: 10.21037/jtd-23-1391
View this article at: https://dx.doi.org/10.21037/jtd-23-1391

Introduction

Aortic stenosis has an estimated prevalence of 3–5% among persons over the age of 75 (1) and is the most common cause for hospitalization due to valvular disease in the developed world (2). Severe symptomatic aortic stenosis is associated with high mortality, which may be prevented by timely valve replacement (3,4). Transcatheter aortic valve replacement (TAVR) is an effective therapy for severe symptomatic aortic stenosis (3,4), however several studies have documented disparities in access to TAVR among different racial and ethnic groups (5,6). Treatment disparities may arise from differences in socioeconomic,

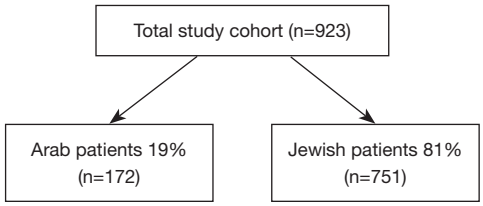

Figure 1 Study flow chart for distribution of study groups.

cultural, immigration-related, and genetic factors, as well as the conscious or unconscious racial bias of health care providers (7).

As of 2021, persons of Arab ethnicity constitute 21% of the population of the state of Israel (8). Despite universal health coverage, Arabs in Israel have poorer healthcare utilization patterns, worse health outcomes and shorter life expectancy than Jews (9-13). However, outcome of TAVR procedures among different demographics within Israeli society is unknown. Therefore, the aim of this study was to characterize the Israeli Arab and Jewish patients undergoing TAVR and compare their post-procedural mortality. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1391/rc).

Methods

Study population

This study utilized the Carmel Medical Center prospective registry, which documents all TAVR procedures performed at this institute. Clinical and procedural data of consecutive patients who underwent TAVR between March 2010 and March 2021 was extracted and analyzed. Survival analysis was performed via a computerized national database. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The institutional review board of Carmel Medical Center approved the study protocol (No. 0029-14), and informed consent was taken from all the patients. We compared baseline demographic, clinical and procedural patient characteristics as well as 7-day, 30-day, and 1-year mortality between Arabs and Jewish patients who underwent TAVR for severe aortic stenosis.

Statistical analysis

Comparison between Jewish and Arab patients was performed using Chi-square (or Fisher's exact test) for categorical variables. For continuous variables, the *t*-test (or Wilcoxon rank-sum test) was used. Univariate and multivariable Cox regression was implemented to compare the hazard for mortality (at 7 days, 30 days and 1 year, separately) between Jews and Arabs. Hazard ratios (HRs) were presented with 95% confidence intervals (95% CIs). In the multivariable Cox regression, adjustments were made for variables that were found significantly different between Jews and Arabs. The statistical analyses were performed using SAS 9.4 software (SAS Institute Inc., Cary, NC, USA). P value <0.05 was considered statistically significant.

Highlight box

Key findings

- Despite Arab subjects having lower-risk characteristics and lower predicted mortality than Jewish patients undergoing transcatheter aortic valve replacement (TAVR), post-procedural mortality was similar in both patient groups.

What is known and what is new?

- Ethnic minorities may face disparities in access to health care and clinical outcomes.
- In a cohort of subjects with severe aortic stenosis referred for TAVR in Israel, Arab patients had lower-risk characteristics and lower predicted mortality compared to Jewish patients.

What is the implication, and what should change now?

- These findings should be verified in larger prospective studies.

Results

The study cohort included 923 subjects [172 (19%) Arabs, 751 (81%) Jews] (*Figure 1*). Baseline patient characteristics are presented in *Table 1*. The Arab patient population was younger (mean 77 *vs.* 81 years, P<0.001), had lower prevalence of coronary artery disease (34%, *vs.* 43%, P=0.02), hypertension (80% *vs.* 88%, P<0.01) and calculated procedural mortality (EuroScore II: mean 4.6 *vs.* 4.9, P=0.02), and higher percentage of females (65% *vs.* 53%, P=0.01), body mass index (mean 30 *vs.* 28, P<0.001) and creatinine clearance (mean 67 *vs.* 59 mL/min, P<0.001).

Jewish and Arab patients had similar comorbidities including smoking (16% *vs.* 15%, P=0.60), diabetes mellitus (40% *vs.* 38%, P=0.67), history of coronary bypass surgery (15% *vs.* 12%, P=0.30), atrial fibrillation (24% *vs.* 23%, P=0.69), peripheral artery disease (8% *vs.* 6%, P=0.28) and previous stroke (9% *vs.* 8%, P=0.60). Moreover, no differences were found in imaging findings by echocardiography or computed tomography angiography.

Table 1 Baseline demographic, clinical and imaging characteristics

Demographic/clinical/imaging characteristics	Jews (n=751)	Arabs (n=172)	P value
Age (years)	81±7 [82]	77±7 [78]	<0.001
Gender, female	401 (53%)	111 (65%)	0.01
Height (cm)	164±10 [164]	164±9 [165]	0.93
Weight (kg)	75±16 [74]	81±18 [80]	<0.001
Body mass index (kg/m^2)	28±6 [27]	30±6 [30]	<0.001
Smoking history	121 (16%)	25 (15%)	0.60
Diabetes mellitus	297 (40%)	65 (38%)	0.67
Hyperlipidemia	590 (79%)	137 (80%)	0.75
Hypertension	660 (88%)	138 (80%)	<0.01
Dialysis	10 (1%)	6 (3%)	0.09
Atrial fibrillation	181 (24%)	39 (23%)	0.69
Pre-existing complete left bundle branch block	169 (23%)	30 (17%)	0.14
Pre-existing permanent pacemaker	60 (8%)	8 (5%)	0.13
Coronary artery disease	325 (43%)	58 (34%)	0.02
Prior coronary bypass surgery	115 (15%)	21 (12%)	0.30
Previous stroke	66 (9%)	13 (8%)	0.60
Chronic lung disease	84 (11%)	18 (10%)	0.78
Peripheral artery disease	62 (8%)	10 (6%)	0.28
Bicuspid aortic valve	42 (6%)	4 (2%)	0.07
Hemoglobin (g/dL)	11.8±1.57 [11.9]	11.8±1.65 [12]	0.97
Hematocrit (%)	36.4±4.47 [36]	36.6±5.38 [37]	0.63
Creatinine (mg/dL)	1.1±0.5 [1.2]	1.1±0.7 [0.94]	0.23
Creatinine clearance (mL/min)†	59.2±23.1 [56]	67.0±26.3 [66]	<0.001
EuroScore II	4.9±4.4 [3.6]	4.6±4.3 [3.2]	0.02
Ejection fraction (%)	56.4±10.1 [60]	56.3±9.2 [60]	0.24
Maximal aortic valve pressure gradient (mmHg)	82.5±23.6 [79]	83.7±23.8 [79]	0.57
Mean aortic valve pressure gradient (mmHg)	51.0±15.8 [48]	50.3±14.7 [47]	0.59
Aortic annulus perimeter (mm)	20.7±9.0 [23.9]	20.2±9.2 [23.6]	0.37
Aortic valve area (cm^2)	0.76±0.15 [0.77]	0.75±0.14 [0.75]	0.64
Average aortic annulus diameter (cm)	23.0±4.9 [23.5]	22.8±5.0 [23.5]	0.56

Data are presented as n (%) or mean ± standard deviation [median]. †, calculated by the Cockcroft-Gault Equation.

Procedural characteristics and outcomes are presented in *Table 2*. Heparin dosage was significantly higher in Arab patients than in Jewish patients (6,500 *vs.* 5,000 mL, P<0.001), which reflected the higher body mass index of this population. There were no differences in the volume of contrast media used, fluoroscopy time, rate of balloon pre- and post-dilatation between, need for pacemaker implantation or number of blood units administered between patient groups. Post-procedural mortality was similar among Jewish and Arab patients (7-day mortality:

Table 2 Procedural characteristics and outcomes

Procedural outcomes	Jews (n=751)	Arabs (n=172)	P value
Valve pre-dilatation	220 (29.2)	46 (26.7)	0.46
Valve post-dilatation	136 (18.1)	25 (14.5)	0.26
New left bundle branch block	95 (12.6)	31 (18.0)	0.06
Permanent pacemaker implantation	101 (13.4)	20 (11.6)	0.78
Contrast volume (mL)	176±66.5 [170]	174±63.5 [170]	0.68
Fluoroscopy time (min)	23.2±10.7 [20.7]	22.5±9.2 [20]	0.39
Heparin dose (mL)	6,186±3,071 [5,000]	6,616±1,840 [6,500]	<0.001
Blood units	0.7±1.5 [0]	0.9±2.3 [0]	0.80
7-day mortality	10 (1.3)	3 (1.7)	0.72
30-day mortality	15 (2.0)	5 (2.9)	0.40
1-year mortality	72 (9.5)	18 (10.5)	0.72

Data are presented as n (%) or mean ± standard deviation [median].

Table 3 Univariate and multivariable Cox regression: mortality among Arab *vs.* Jewish patients undergoing transcatheter aortic valve replacement

Mortality (Arab *vs.* Jews)	HR			Adj. HR		
	Value	95% CI	P value	Value	95% CI	P value
Mortality in 7 days	1.31	0.36–4.76	0.6828	1.51	0.39–5.77	0.55
Mortality in 30 days	1.46	0.53–4.02	0.4627	1.79	0.62–5.18	0.29
Mortality in 1 year	1.1	0.66–1.84	0.7183	1.24	0.72–2.12	0.43

Adjustments were made for: age, gender, BMI, creatinine clearance, hypertension, coronary artery disease and EuroScore II. HR, hazard ratio; adj. HR, adjusted HR; CI, confidence interval; BMI, body mass index.

1.3% *vs.* 1.7%, P=0.72; 30-day mortality: 2.0% *vs.* 2.9%, P=0.40; 1-year mortality: 9.5% *vs.* 10.5%, P=0.72).

Univariate survival analysis (Cox regression) demonstrated no significant difference in the risk for 7-day, 30-day and 1-year mortality between Jewish and Arab patients undergoing TAVR (*Table 3*). As there were significant differences between Jews and Arabs in demographic and clinical factors, multivariable Cox regression was performed as well. Although Arab patients were younger and had lower predicted procedural risk, after adjusting for age, gender, body mass index, creatinine clearance, hypertension, coronary artery disease, and EuroScore II, they still had similar post-procedural mortality compared to Jewish patients (7-day mortality: adjusted HR 1.51, 95% CI: 0.39–5.77, P=0.55; 30-day mortality: adjusted HR 1.79, 95% CI: 0.62–5.18, P=0.29; 1-year mortality: adjusted HR 1.24, 95% CI: 0.72–2.12, P=0.43).

Discussion

In a cohort of subjects with severe aortic stenosis referred for TAVR in Israel, Arab patients had lower-risk characteristics and lower predicted mortality compared to Jewish patients, however these characteristics did not translate into improved post-procedural survival.

Ethnic disparities in the presentation and outcome of cardiovascular disease over the world have been attributed to variability in the prevalence of cardiovascular risk factors, differences in screening for primary prevention, poor health literacy, healthcare-seeking behaviors, and compliance to treatment among specific ethnicities (14). Before the introduction of TAVR, Black individuals in the United States were significantly less likely to receive aortic

valve replacement compared to Whites (39% *vs.* 53%, P=0.04) (15). Analysis of the Society of Thoracic Surgeons Transcatheter Valve Therapy (STS TVT) Registry covering the post-TAVR introduction period from 2011 to 2016 revealed under-representation of Black individuals among those receiving transcatheter therapies (16,17).

Despite universal health coverage, Arabs in Israel have poorer healthcare utilization patterns, worse health outcomes and shorter life expectancy than Jews (9-13). Several previous studies reported that Israeli Arabs were at increased risk for coronary events (18) and presented at a younger age than Israeli Jews with acute myocardial infarction or heart failure (19-20). In the present study, the percentage of Arab patients undergoing TAVR procedures within the total study cohort reflected the relative size of this ethnic segment within Israeli society. The fact that lower-risk characteristics of Arab patients did not result in decreased mortality may have several explanations. It is possible that Arab subjects had co-morbidities that were not identified in the present study which may have adversely affected their clinical outcome. The higher percentage of female subjects within the Arab subgroup may have impacted the findings, as some studies have noted increased mortality among females undergoing TAVR (21). Arab subjects had increased body mass index which may have contributed to patient-prosthesis mismatch, which is associated with worse clinical outcome. Life-course adversity through epigenetic processes is one potential mechanism which may have prevented the lower risk profile of Arabs undergoing TAVR from translating into more favorable clinical outcome.

While our study demonstrated valuable insights, it is important to acknowledge its limitations. This research was conducted at a single center in northern Israel, potentially lacking the statistical power to discern subtle outcome differences within the study subgroups. A multi-center study spanning different regions of the country may provide a more comprehensive representation of disparities between ethnic groups on a national scale.

Conclusions

Despite Arab subjects having lower-risk characteristics and lower predicted mortality than Jewish patients undergoing TAVR, post-procedural mortality was similar in both patient groups. These findings should be verified in larger prospective studies.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1391/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1391/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1391/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1391/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The institutional review board of Carmel Medical Center approved the study protocol (No. 0029-14), and informed consent was taken from all the patients.

References

1. Eugène M, Duchnowski P, Prendergast B, et al. Contemporary Management of Severe Symptomatic Aortic Stenosis. J Am Coll Cardiol 2021;78:2131-43.
2. Yadgir S, Johnson CO, Aboyans V, et al. Global, Regional, and National Burden of Calcific Aortic Valve and Degenerative Mitral Valve Diseases, 1990-2017.

Circulation 2020;141:1670-80.
3. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2021;143:e72-e227.
4. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J 2022;43:561-632.
5. Brennan JM, Lowenstern A, Sheridan P, et al. Association Between Patient Survival and Clinician Variability in Treatment Rates for Aortic Valve Stenosis. J Am Heart Assoc 2021;10:e020490.
6. Yong CM, Jaluba K, Batchelor W, et al. Temporal trends in transcatheter aortic valve replacement use and outcomes by race, ethnicity, and sex. Catheter Cardiovasc Interv 2022;99:2092-100.
7. Batchelor W, Anwaruddin S, Ross L, et al. Aortic Valve Stenosis Treatment Disparities in the Underserved: JACC Council Perspectives. J Am Coll Cardiol 2019;74:2313-21.
8. Israel Central Bureau of Statistics. Statistical abstract of Israel 2015. 66 ed Jerusalem: Israel Central Bureau of Statistics; 2016. Available online: http://www.cbs.gov.il/reader/shnaton/shnatone_new.htm. Accessed 19 Feb 2018.
9. Daoud N, Soskolne V, Mindell JS, et al. Ethnic inequalities in health between Arabs and Jews in Israel: the relative contribution of individual-level factors and the living environment. Int J Public Health 2018;63:313-23.
10. Karkabi B, Zafrir B, Jaffe R, et al. Ethnic Differences Among Acute Coronary Syndrome Patients in Israel. Cardiovasc Revasc Med 2020;21:1431-5.
11. Muhsen K, Green MS, Soskolne V, et al. Inequalities in non-communicable diseases between the major population groups in Israel: achievements and challenges. Lancet 2017;389:2531-41.
12. Saabneh AM. Arab-Jewish gap in life expectancy in Israel. Eur J Public Health 2016;26:433-8.
13. Chernichovsky D, Anson J. The Jewish-Arab divide in life expectancy in Israel. Econ Hum Biol 2005;3:123-37.
14. Vaduganathan M, Mensah GA, Turco JV, et al. The Global Burden of Cardiovascular Diseases and Risk: A Compass for Future Health. J Am Coll Cardiol 2022;80:2361-71.
15. Yeung M, Kerrigan J, Sodhi S, et al. Racial differences in rates of aortic valve replacement in patients with severe aortic stenosis. Am J Cardiol 2013;112:991-5.
16. Alkhouli M, Alqahtani F, Holmes DR, et al. Racial Disparities in the Utilization and Outcomes of Structural Heart Disease Interventions in the United States. J Am Heart Assoc 2019;8:e012125.
17. Alkhouli M, Holmes DR Jr, Carroll JD, et al. Racial Disparities in the Utilization and Outcomes of TAVR: TVT Registry Report. JACC Cardiovasc Interv 2019;12:936-48.
18. Kark JD, Fink R, Adler B, et al. The incidence of coronary heart disease among Palestinians and Israelis in Jerusalem. Int J Epidemiol 2006;35:448-57.
19. Harpaz D. Ethnic differences in mortality of male and female patients surviving acute myocardial infarction: long-term follow-up of 5,700 patients. The Secondary Prevention Reinfarction Israeli Nifedipine Trial (SPRINT) Study Group. Eur J Epidemiol 1997;13:745-54.
20. Gotsman I, Avishai-Eliner S, Jabara R, et al. Ethnic disparity in the clinical characteristics of patients with heart failure. Eur J Heart Fail 2015;17:801-8.
21. Trongtorsak A, Thangjui S, Adhikari P, et al. Gender Disparities after Transcatheter Aortic Valve Replacement with Newer Generation Transcatheter Heart Valves: A Systematic Review and Meta-Analysis. Med Sci (Basel) 2023;11:33.

Cite this article as: Sliman H, Eitan A, Shiran A, Zafrir B, Karkabai B, Flugelman MY, Schwartz N, Jaffe R. Outcome of transcatheter aortic valve replacement in Israeli Jews and Arabs. J Thorac Dis 2024;16(1):241-246. doi: 10.21037/jtd-23-1391