Implantable Loop Recorders in Patients with Unexplained Syncope: Does Ethnic Background Influence Diagnostic Yield?

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ABSTRACT **Background:** Implantable loop recorders (ILRs) are a central tool in the evaluation of unexplained syncope. These devices record and store electrocardiograms, both automatically and on patient-dependent activation. Therefore, obtaining optimal diagnostic results relies on a patient's comprehension and collaboration.

Objectives: To evaluate the effect of ethnic background and mother-tongue language on the diagnostic yield (DY) of ILRs.

Methods: Patients at two medical centers in Israel, who had ILRs as part of syncope workup were included. Inclusion criteria were age over 18 years and an ILR for at least one year (or less if the cause of syncope was detected). Patient demographics, ethnic background, and previous medical history were recorded. All findings from ILR recordings, activation mode (manual vs. automatic), and treatment decisions (none, ablation, device implantation) were collected.

Results: The study comprised 94 patients, 62 Jews (i.e., ethnic majority) and 32 non-Jews (i.e., ethnic minority). While baseline demographic characteristics, medical history, and drug therapy were similar in both groups, Jewish patients were significantly older at the time of device implantation: 64.3 ± 16.0 years of age vs. 50.6 ± 16.9, respectively; ($P < 0.001$). Arrhythmias recorded in both groups as well as treatment decisions and device activation mode were similar. Total follow-up time from device implantation was longer in the non-Jewish vs. the Jewish group (17.5 ± 12.2 vs. 24.0 ± 12.4 months, respectively; $P < 0.017$).

Conclusions: The DY of ILR implanted for unexplained syncope did not seem to be influenced by patient's mother-tongue language or ethnicity.

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KEY WORDS: diagnostic yield, ethnicity, implantable loop recorders (ILR), syncope

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Syncope is common in the general population and associated with reduced quality of life and significant economic burden to healthcare systems. Therefore, a structured and organized, evidence-based protocol for diagnosis of syncope is needed [1]. Implantable loop recorders (ILRs) are important diagnostic tools in syncope workup. They offer long standing continuous high fidelity electrocardiogram recording, thereby increasing diagnostic yield.

The 2018 European Society of Cardiology guidelines for diagnosis and management of syncope [2] highlighted the use of ILRs and recommended their use in diagnostic workups. Although initial implantation costs are high, if a symptom–electrocardiogram correlation can be achieved, then analysis of the cost per symptom–electrocardiogram yield has shown that the implanted device may be more cost-effective than a strategy using conventional investigation [3].

Recoding of arrhythmias or arrhythmia-suspected events occur in one of two ways: automatically triggered in the case of predefined arrythmias or patient/bystander-triggered usually following syncope; therefore, patient education regarding device activation is essential.

We evaluated whether ethnic background and mother-tongue language other than the main language, which may result in language barrier, may influence diagnostic yield (DY) of ILRs in a multi-ethnic population.

PATIENTS AND METHODS

This study was conducted in northern Israel, a region known for its ethnic diversity, and home to Jews, Arabs (Muslim and Christians), Druse, and others. For practical reasons, we assumed that the mother tongue of Jewish patients was Hebrew (main language), while non-Jewish minorities had a mother tongue other than Hebrew (mainly Arabic). Data were collected prospectively collected from two public hospitals, Ziv Medical Center and Tzafon Medical Center, which serve a local population of about 500,000 people. Information on all patients who underwent ILR implantation between January 2015 and December 2020 as part of syncope workup was collected.

Patients were eligible for inclusion in the trial if they were over 18 years of age and had device implantation as part of syncope evaluation. Data from earlier diagnostic studies (such as tilt-test, Holter electrocardiogram, Carotid sinus massage, tests for orthostatic hypotension or similar) were not available and were therefore not recorded in the current results. A follow-up time of no less than 12 months following ILR implantation at the medical centers was required (or less if the cause of syncope was detected). As per local practice, patients were summoned twice per year for device monitoring and for any event of syncope or self-activated, symptom-initiated recording. Patient medical and cardiovascular history records, current medication, electrocardiogram characteristics at implantation, and ethnic background were collected. The study protocol was approved by the institutional review boards of both medical centers.

For each participant, total follow up time (i.e., from ILR implantation to its removal, end of trial, pacemaker implantation, electrophysiology study, or last visit), diagnostic yield, and treatment were recorded. For the current trial, DY was defined as any arrhythmia detected by the ILR. Therefore, all arrhythmias were documented even if unlikely to cause syncopal event (e.g., supraventricular tachycardias). All clinical decisions, including the indication for ILR, initiation of anticoagulation, or pacemaker insertion, were at the discretion of the treating cardiologist.

RESULTS

In total, 94 patients were enrolled in the study. Of these, 62 were Jewish and 32 were non-Jewish [Table 1]. Ninety-three devices were Medtronic Reveal™ XT/DX (Medtronic, Ireland) and one was Biotronik BioMonitor 2 (Biotronik, Germany). The non-Jewish population included Druze, Muslims, and Christians, all with Arabic as their mother-tongue language. While no difference was noted between the two groups in terms of gender and body mass index (BMI), the Jewish population was significantly older at the time of device implantation: 64.3 ± 16.0 years of age vs. 50.6 ± 16.9, respectively ($P < 0.001$).

The medical history of both groups, including cardiovascular disease as well as relevant risk factors such as diabetes, arterial hypertension, kidney failure, and hyperlipidemia, were well balanced. Drug therapy including use of statins, beta blockers, antiplatelets, and renin-angiotensin blockers, was similar in both groups [Table 2]. Baseline electrocardiogram findings were similar for both populations.

Although ILR findings in both groups were similar [Table 3], numerically more Jewish patients were diagnosed with atrial arrhythmias (fibrillation/flutter) and atrioventricular block. This result led to a numerically higher portion of Jewish patients undergoing electrophysiological ablation and device implantation, resulting in a shorter total follow-up time for the Jewish population (17.5 ± 12.2 vs. 24.0 ± 12.4 months, respectively; $P < 0.017$).

Device activation mode (automated vs. manual recording)

Table 1. Demographic characteristics according to ethnic group

	Jews (ethnic majority) (n=62)	Others (ethnic minority) (n=32)	*P*-value
Ethnicity sub-group, n (%)			
Druze	–	16 (50.0)	
Muslim	–	15 (46.9)	
Christian	–	1 (3.1)	
Gender (n, %)			
Female	35 (56.5)	12 (37.5)	0.082
Male	27 (43.5)	20 (62.5)	
Age in years, mean	64.3 ± 16.0	50.6 ± 16.9	< 0.001
Body mass index, kg/m^2 (mean ± SD)	28.4 ± 5.8	28.0 ± 7.3	0.797

SD = standard deviation

Table 2. Risk factors, drug therapy, and baseline electrocardiogram findings

	Jews (ethnic majority) (n=62)	Others (ethnic minority) (n=32)	*P*-value
eGFR MDRD, ml/min (mean ± SD)	75.8 ± 22.8	86.0 ± 28.5	0.095
Hemoglobin, gr/dl (mean ± SD)	13.3 ± 1.6	13.4 ± 2.0	0.867
Creatinine, mg/dl (mean ± SD)	0.95 ± 0.25	1.16 ± 1.32	0.290
Cerebrovascular disease, any (n, %)	5 (9.1)	3 (10.7)	0.547
Hypertension, n (%)	39 (66.1)	14 (45.2)	0.055
Smoking history, n (%)	6 (12.5)	7 (25.9)	0.140
Diabetes mellitus, n (%)	16 (28.1)	12 (40.0)	0.258
Hyperlipidemia, n (%)	32 (55.2)	15 (48.4)	0.541
Coronary artery disease, n (%)	14 (28.0)	8 (27.6)	0.968
Ejection fraction, mean ± SD	59.6 ± 7.6	60.0 ± 8.4	0.842
Drug therapy, n (%)			
ACE* / ARB	25 (43.9)	12 (40.0)	0.729
Beta blockers	19 (33.3)	9 (31.0)	0.830
Statins	27 (48.2)	14 (46.7)	0.891

ACE = angiotensin-converting enzyme inhibitors, ARB = angiotensin II receptor blockers, GFR = glomerular filtration rate, MDRD = modification of diet in renal disease, SD = standard deviation

Table 3. ILR findings and follow-up treatment

	Jews (ethnic majority) (n=62)	Others (ethnic minority) (n=32)	*P*-value
Diagnostic yield, n (%)			
None	28, 45.2	19, 59.4	0.478
Atrial flutter / fibrillation	15, 24.2	4, 12.5	
Sinus node dysfunction	9, 14.5	5, 15.6	
Atrioventricular block / Asystole	10, 16.1	4, 12.5	
Treatment, n (%)			
None	42, 67.7	27, 84.4	0.433
Device implantation	13, 21.0	3, 9.4	
Ablation	3, 4.8	1, 3.1	
Anticoagulation	4, 6.5	1, 3.1	
Total follow-up, months (mean ± sd)	17.5±12.2	24.0±12.4	0.017
ILR mode of activation, n (%)			
Automatic	10, 47.6	6, 66.7	0.440
Manual	11, 52.4	3, 33.3	

ILR = Implantable loop recorder, SD = standard deviation

was also recorded for those individuals with documented arrhythmia. Although data were not available for all patients (21 Jewish and 9 non-Jewish), events were recorded in an even manner for the Jewish group. For the non-Jewish minority most recordings (67%) were automatically activated, a difference that was not statistically significant ($P = 0.44$).

DISCUSSION

Results of the current study did not indicate any ethnic or language-related influence on ILR diagnostic yield in the population tested.

The Galilee and Golan Heights regions, located in northern Israel, are known for their diverse ethnic demography and are therefore ideal for studies evaluating the influence of ethnic and cultural backgrounds. While previous research has revealed a gap in cardiovascular health and life expectancy between Jews and Arabs in Israel [4,5], current knowledge regarding disparities in ILR-assisted syncope diagnosis between those groups is lacking. Thus, the current study was constructed to fill this gap.

To the best of our knowledge, this research is the first to examine this subject. Although recording is automatically activated in ILRs in the event of arrhythmia, patients are instructed to activate recording in case of syncope or when symptoms occur. Thus, ethnic background characterized by a different mother-tongue than the language designated as the country's prominent language and therefore used in a public hospital, may cause a language barrier and lead to alterations in device-activation comprehension between populations, with eventual impact on DY.

The DY of loop recorders is considered high and was evaluated in several trials, including in Israel [6]. The ISSU-2 group reported successful, effective, and safe ILR-based therapy specific for patients with neurally-mediated syncope [7]. Furthermore, 33% of patients had an electrocardiogram diagnosis following 276 ± 134 days of ILR implantation in the EaSyAS trial [8]. However, a recently published study reported a yield lower than 30% [9]. This discrepancy may be related to the trend in recent clinical practice to implant ILR at earlier stages of syncope diagnostic workup [10], without invasive electrophysiology studies or outpatient mobile cardiac telemetry monitoring [9], or because devices are placed for indications other than syncope [9].

The PICTURE registry, with 570 patients, is the largest database of patients with recurrent unexplained syncope/pre-syncope from 10 European countries and Israel [11]. The registry revealed that a high number ILR-related diagnostic (78%) events occurred during follow-up and three-quarters were cardiac events. In the current trial, the diagnostic yield was modest. In 45% and 60% of the Jewish and non-Jewish populations, respectively, no arrhythmia was recorded. Modern ILRs have a longevity of 3 years and total follow-up time in our study was limited to 17.5 and 24 months, respectively. A longer follow-up duration might have resulted in improved DY. The PICTURE registry reported a syncopal recurrence rate of 38% during 10 ± 6 months follow-up, which may suggest a higher or similar rate when follow-up is longer (as in our study). However, we did not record recurrences and therefore no clear conclusions can be drawn. Furthermore, such recording might have shed more light on those syncopal episodes that are non-arrhythmia-driven, such as vasovagal events (when ILR-interrogation remains uneventful). Our findings may represent the current practice in which ILRs are implanted early while foregoing other tests, thereby leading to a lower ILR-based diagnosis.

Although the DY of both groups was similar [Table 3], our findings suggest a higher chance of interventions (ablation or device implantation) for the Jewish population. Since the collected raw data for the current work included both printouts from ILR- interrogation or only a summary of the interrogation findings (as documented by the physician on the device follow-up dedicated card), we can only speculate the reasons to proceed or not proceed toward device implantation or electrophysiology study. Most likely, the findings merely represent a matter of chance rather than a true difference.

The results of our research are novel, as no other study, to the best of our knowledge, has evaluated possible correlation between ethnicity (i.e., mother-tongue language) and ILR diag-

nostic yields. As ethnicity does not seem to influence diagnostic success, several explanations may be relevant: Modern ILR allows for a long-term follow-up time and automatic arrhythmia recording in the case of meaningful brady or tachy arrhythmias; therefore, the significance of patient-initiated recording might be limited. Furthermore, all medical services in Israel (hospitals included) must, by law, provide services to patients in a language and manner they can comprehend (Patient's Right Law 1996). In addition, since both the Ziv and Tzafon medical centers employ a large number of non-Jewish staff who speak a language other than Hebrew as their mother tongue, a language barrier may be of no significance. Therefore, the combination of modern, well configured devices and adequately informed ILR-implanted patients seems to nullify any ethnic and language influence.

LIMITATIONS

The current study has several limitations. Its small size may limit the validity of our findings; however, small-size samples, several dozen to a few hundred patients, are common in studies evaluating the usefulness of ILR in diagnosing syncope of unknown cause. Also, the ethnic diversity in our region is unusual. Although inclusion of a larger group of participants is possible, recruiting more patients with similar ethnical background to those included here, poses a major challenge even in Israel. This trial was conducted as an observational study with few exclusion criteria and decision-making left to the discretion of local cardiologists. Recurrent syncope or documentation of pre-ILR diagnostic evaluation were not an inclusion criterion. This real-world all-comers study comes with a price of eventually including patients who did not have an indication for ILR, thereby leading to a modest diagnostic yield. However, such an approach probably truly reflects current practice, including early use of ILRs as endorsed by international guidelines. Last, for practical reasons we assumed that Jewish patients were all native Hebrew speakers while non-Jewish patients were not. While this assumption is true for most participants, it may not be the case for Jewish immigrants or for those from multi-ethnic/multilingual houses.

CONCLUSIONS

The DY of ILRs implanted for clarifying syncopal events does not seem to be influenced by the patent's ethnic group or mother-tongue language.

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The happiest is the person who suffers the least pain;
the most miserable who enjoys the least pleasure.
Jean-Jacques Rousseau (1712–1778), Genevan philosopher, writer, and composer

There is a beauty in discovery. There is mathematics in music, a kinship of science and poetry in the description of nature, and exquisite form in a molecule. Attempts to place different disciplines in different camps are revealed as artificial in the face of the unity of knowledge. All literate men are sustained by the philosopher, the historian, the political analyst, the economist, the scientist, the poet, the artisan, and the musician.
Glenn T. Seaborg (1912–1999), American chemist, Nobel laureate