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Effectiveness, utilisation and cost associated with implantable loop recorders versus external monitors after ischaemic or cryptogenic stroke

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ABSTRACT

Objective Implantable loop recorders (ILRs) are increasingly used for long-term rhythm monitoring after ischaemic and cryptogenic stroke, with the goal of detecting atrial fibrillation (AF) and subsequent initiation of oral anticoagulation to reduce risk of adverse clinical outcomes. There is a need to determine the effectiveness of different rhythm monitoring strategies in this context.

Methods We conducted a retrospective cohort analysis of individuals with commercial and Medicare Advantage insurance in Optum Labs Data Warehouse who had incident ischaemic or cryptogenic stroke and no prior cardiovascular implantable electronic device from 1 January 2016 to 30 June 2021. Patients were stratified by rhythm monitoring strategy: ILR, long-term continuous external cardiac monitor (>48 hours to 30 days) or Holter monitor (≤48 hours). The primary outcome was risk-adjusted all-cause mortality at 12 months. Secondary outcomes included new diagnosis of AF and oral anticoagulation, bleeding, and costs.

Results Among 48 901 patients with ischaemic or cryptogenic stroke, 9235 received an ILR, 29 103 long-term continuous external monitor and 10 563 Holter monitor only. Mean age was 69.9 (SD 11.9) years and 53.5% were female. During the 12-month follow-up period, patients who received ILRs compared with those who received long-term continuous external monitors had a higher odds of new diagnosis of AF and oral anticoagulant initiation (adjusted OR 2.27, 95% CI 2.09 to 2.48). Compared with patients who received long-term continuous external monitors, those who received ILRs had similar 12-month mortality (HR 1.00; 95% CI 0.89 to 1.12), with approximately $13 000 higher costs at baseline (including monitor cost) and $2500 higher costs during 12-month follow-up.

Conclusions In this large real-world study of patients with ischaemic or cryptogenic stroke, ILR placement resulted in more diagnosis of AF and initiation of oral anticoagulation, but no difference in mortality compared with long-term continuous external monitors.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ There is increased interest in monitoring patients with ischaemic or cryptogenic stroke for occult atrial fibrillation (AF), with the goal of detecting this arrhythmia and using oral anticoagulation for secondary stroke prevention.

⇒ Monitoring is increasingly performed using implantable loop recorders (ILRs), but there are no clinical outcomes data to support this practice.

WHAT THIS STUDY ADDS

⇒ This retrospective cohort study found that use of ILRs after ischaemic or cryptogenic stroke led to greater detection of AF and prescription of oral anticoagulation compared with long-term continuous external monitors (>48 hours to 30 days).

⇒ However, there was no statistically significant difference in mortality compared with long-term continuous external monitors.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The results of this study indicate an urgent need for randomised clinical trials to study ILRs in secondary stroke prevention.

INTRODUCTION

Stroke is the fifth leading cause of death in the USA and a leading cause of long-term disability.[1] Cryptogenic strokes, those of uncertain aetiology, comprise 10%–40% of all ischaemic strokes.[2] One possible aetiology of cryptogenic stroke is subclinical atrial fibrillation (AF). A new diagnosis of AF after stroke is associated with an increased risk of recurrent stroke,[3] and these strokes result in greater morbidity and mortality.[4]

Accordingly, there has been interest in monitoring for AF among patients with cryptogenic stroke, based on the hypothesis that detection of occult AF and the use of oral anticoagulation could reduce risk of recurrent stroke and subsequent disability and mortality.[5] Strategies for AF detection include continuous external monitors and implantable loop recorders (ILRs). The 2021

American Heart Association/American Stroke Association clinical practice guideline for secondary prevention of ischaemic stroke gives a Class 2a recommendation for long-term rhythm monitoring to detect intermittent AF among patients with cryptogenic stroke; this is a moderate recommendation in which benefits are considered to outweigh risks.[6] This guideline recommendation is based on three clinical trials with the surrogate endpoint of AF detection as the primary endpoint, not on clinical outcomes such as reduction in recurrent stroke or mortality.[7–9]

Given that cardiac monitoring after stroke leads to the identification of more AF, it leads to more initiation of oral anticoagulation, especially for long-term monitors such as ILRs.[10–12] However, reduction in all-cause mortality has not been demonstrated.[10–12] Simultaneously, clinical trial evidence suggests that screening with ILRs among patients with increased risk of stroke (but not necessarily prior stroke) compared with usual care results in threefold higher AF detection and anticoagulant use, but no significant reduction in stroke.[13] The additional use of anticoagulation could increase bleeding risk.[14]

There is a paucity of real-world data in large datasets addressing if long-term cardiac monitoring with ILRs improves clinical outcomes in a secondary stroke prevention setting. Despite the lack of evidence, there has been growth in use of ILRs in recent years, and ILR placement after stroke is the third most common indication for ILR use.[15] Accordingly, in this study, we asked: what are outcomes associated with use of ILRs compared with non-invasive rhythm monitoring among patients with recent ischaemic or cryptogenic stroke? Given that ILRs represent a costly, implanted technology, we also sought to understand differences in healthcare expenditures.

METHODS

Study design and data source

This retrospective cohort analysis of de-identified administrative claims data used the Optum Labs[16] Data Warehouse (OLDW) for commercial and Medicare Advantage enrollees, which includes medical claims, pharmacy claims and enrolment records, and where applicable contains mortality information at month and year. OLDW contains longitudinal health information on enrollees, representing a mixture of ages and geographical regions across the USA. Because data were de-identified in compliance with the Health Insurance Portability and Accountability Act, an Institutional Review Board review or waiver of authorisation was not required.[17] This study followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines. Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Cohort selection

We created a cohort of individuals who received outpatient cardiac rhythm monitoring between 1 January 2016 and 30 June 2021. Patients were stratified into two groups, those with ILR placement and those who did not have an ILR but had either long-term continuous external cardiac monitoring (>48 hours to 30 days) or Holter monitoring (≤48 hours) (online supplemental table 1). Patients were stratified hierarchically based on the earliest date of a claim for an ILR, long-term continuous external cardiac monitor or Holter (and in that order). In other words, those who were classified as Holter could not have either an ILR or long-term continuous external cardiac monitor during their baseline period. Those classified as ILR or long-term continuous external cardiac monitor could have had the lower hierarchy device during baseline (long-term continuous external cardiac monitor or Holter for ILR and only Holter for the long-term continuous external cardiac monitor group).

The date of ILR insertion or earliest claim date for other monitors was the index date. Patients with an index date during an inpatient hospitalisation had the date adjusted to their hospital discharge date. This ensured that for all three groups, device-related inpatient utilisation and cost were consistently captured during the baseline period, which included the index date and 6 months prior to it.

All included patients were required to meet the following criteria during the 6 months prior to placement of the index monitoring device: (1) either cryptogenic or ischaemic stroke diagnosis (online supplemental table 2)[15 18]; (2) continuous enrolment with medical and pharmacy coverage; (3) no evidence of pacemaker, implantable cardioverter-defibrillator, cardiac resynchronisation therapy, AF ablation, atrioventricular node ablation or left atrial appendage occlusion (online supplemental table 3); (4) no pharmacy claims for warfarin or direct oral anticoagulants (online supplemental table 4); (5) no evidence of complete heart block, haemorrhagic stroke or CHA_2DS_2-VASc (1 point for congestive heart failure, 1 point for hypertension, 1 point for diabetes mellitus, 2 points for ischaemic stroke/transient ischaemic attack/thromboembolism, 1 point for vascular disease, 1 point for age 65–74 years, 2 points for age ≥75 years and 1 point for female sex) score[19] ≤1; and (6) no data anomalies, including missing demographic information (age, sex) or a date of death earlier than index date. All patients were also required to have ≥3 months ILR-free period prior to the index monitoring device (online supplemental table 1).

Outcomes

The primary outcome was all-cause mortality based on month of death from 1 day postindex through 12 months of follow-up. For the analysis of time to month of death, beneficiaries were censored at disenrolment or month of death, whichever occurred earlier.

Secondary outcomes included clinical, safety, healthcare utilisation and cost outcomes. Clinical outcomes

were a new diagnosis of AF (online supplemental table 2) and initiation of oral anticoagulants. Although we examined multiple outcomes on the causal path of secondary stroke prevention, including new AF diagnosis and anticoagulation as well as mortality, we did not include recurrent ischaemic or cryptogenic stroke because of a lack of sufficient accuracy of claims diagnoses and potentially differential misclassification.[20] Safety outcomes were haemorrhagic stroke, major gastrointestinal bleeding and minor bleeds (online supplemental table 5). Healthcare utilisation outcomes were emergency department (ED) visits, hospitalisations, cumulative number of inpatient days and office visits. Cost outcomes were total costs of care, medical costs, outpatient pharmacy costs and direct medical costs of the monitoring devices; costs are summarised as both total and per member per month (PMPM). All were actual paid costs, which were adjusted to 2020 values using the Consumer Price Index. To assess secondary outcomes, all patients were required to have ≥12 months of continuous medical and pharmacy coverage following the index date; patients who died within the first 12 months were not included in assessment of secondary outcomes. Follow-up was assessed starting the day after the index date.

Covariates

CHA_2DS_2-VASc score was used for risk adjustment based on comorbidity burden and its association with adverse outcomes among patients with AF.[21] Comorbidities were coded using facility and physician medical claims during the 6-month baseline period.

Statistical analysis

Cohort characteristics were summarised overall and for three study groups (ILR, long-term continuous external monitoring, Holter monitoring). Categorical variables are described as counts and percentages, and count and continuous variables are summarised as mean with SD or median with IQR. Pair-wise unadjusted significance of differences were assessed by either general linear model F statistic for continuous variables or χ^2 for categorical variables.

All-cause mortality was modelled as time-to-event using Cox proportional hazards regression with the exposure group as the primary predictor. Binary and cost outcomes were modelled using logistic regression and generalised linear models with a gamma distribution and logarithmic link. All models were further adjusted for CHA_2DS_2-VASc groups.

Additionally, given that patients in long-term care may be at higher risk for adverse outcomes, we conducted a subanalysis excluding patients who had long-term care stays of ≥45 days during the 6-month baseline period. We also conducted a subanalysis excluding patients who had received a previous monitoring device (ie, limiting to just the first monitoring device that a given patient received).

All analyses were performed using SAS Enterprise Guide, V.7.1.

RESULTS

Baseline patient characteristics

The cohort of 48 901 individuals included 9235 patients with ILR, 29 103 with long-term continuous external monitor (>48 hours to 30 days), and 10 563 with Holter monitor only (≤48 hours); this cohort was used to assess all-cause mortality (online supplemental figure 1). In the overall cohort, the mean age was 69.9 (SD 11.9) years and 53.5% of patients were female (table 1). Overall, 8451 (17.3%) patients had an index date of device placement during an inpatient stay. In the 6-month baseline period, 5.1% of patients had a Holter monitor (6.3% prior to long-term continuous external monitor placement and 7.4% prior to ILR placement) and 4.2% had an external monitor. The mean CHA_2DS_2-VASc score was 5.3 (SD 1.5).

After limiting to patients with at least 12 months of continuous enrolment, the cohort of patients to assess healthcare utilisation, costs and clinical outcomes included 6904 patients with ILRs, 22 079 with long-term continuous external monitors and 7916 with Holter monitors only. Baseline patient characteristics were similar to those in the cohort used to examine mortality (online supplemental table 6).

Unadjusted outcomes of ILRs versus external monitors

Mortality

Unadjusted mortality was not statistically different among the three patient groups: 4.2% of patients with ILRs, 4.2% with long-term continuous external monitors and 4.7% of patients with Holter monitors had died at 12 months (p=0.053) (online supplemental table 7 and figure 2). Unadjusted mortality was similar for patients with <45 days of long-term care during the baseline period and among those who had no baseline history of a prior rhythm monitoring device (online supplemental table 8).

Clinical outcomes

In unadjusted analyses, 23.2% of patients with ILRs, 13.7% with long-term continuous external monitors and 8.2% with Holter monitors were diagnosed with new AF at 12 months (p<0.001) (online supplemental table 9). Similarly, new initiation of oral anticoagulants was 25.5% in the ILR group, 13.4% in the long-term continuous external monitor group and 9.0% in the Holter group (p<0.001).

Twelve-month major gastrointestinal bleeding was not statistically different between the groups, while haemorrhagic stroke was higher among patients with ILRs (2.5% vs 1.6% vs 1.4%, respectively; p<0.001).

After the index date, 25.3% of patients with ILRs, 22.8% with long-term continuous external monitors and 22.4% with Holter monitors were hospitalised within 12 months (p<0.001, online supplemental table 10). Patients with ILRs also more often had at least one ED visit (46.9% vs 45.6% vs 43.7%, respectively, p<0.001) and a higher mean total number of office visits (24.9 vs 18.3 vs 18.0, respectively, p<0.001).

Table 1 Baseline characteristics

	Total		Implantable loop recorder		Long-term continuous external monitor		Holter monitor		Global p value
	N	%	N	%	N	%	N	%	
Cohort N	48 901	100	9235	18.9	29 103	59.5	10 563	21.6	
Age, years (mean, SD)	69.9	11.9	69.6	11.4	69.8	12.0	70.5	12.0	<0.001
Gender									
Female	26 148	53.5	4688	50.8	15 729	54.1	5731	54.3	<0.001
Male	22 753	46.5	4547	49.2	13 374	46.0	4832	45.7	<0.001
Insurance type									
Commercial	12 417	25.4	2477	26.8	7567	26.0	2373	22.5	<0.001
Medicare Advantage	36 469	74.6	6754	73.2	21 526	74.0	8189	77.5	<0.001
Index device year									
2016	5759	11.8	885	9.6	2934	10.1	1940	18.4	<0.001
2017	7657	15.7	1311	14.2	4205	14.5	2141	20.3	<0.001
2018	9200	18.8	1857	20.1	5245	18.0	2098	19.9	<0.001
2019	11 081	22.7	2189	23.7	6834	23.5	2058	19.5	<0.001
2020	10 610	21.7	1971	21.3	7158	24.6	1481	14.0	<0.001
2021	4594	9.4	1022	11.1	2727	9.4	845	8.0	<0.001
Monitoring device placement setting									
Monitoring device placement date between a hospitalisation and discharge	8451	17.3	3777	40.9	3748	12.9	926	8.8	<0.001
Monitoring device placement same day as emergency department visit	4762	9.7	2556	27.7	1670	5.7	536	5.1	<0.001
Procedures of interest									
Holter monitor utilisation during 6 months prior to index device placement	2502	5.1	681	7.4	1821	6.3	0	0	<0.001
External cardiac monitor utilisation during 6 months prior to index device	2043	4.2	>2031*	>21.0*	0	0	<11*	<0.1*	<0.001
CHA_2DS_2-VASc score and comorbidities (based on 6-month baseline period†)									
Heart failure	7772	15.9	1565	17.0	4467	15.4	1740	16.5	<0.001
Hypertension	42 146	86.2	8238	89.2	24 916	85.6	8992	85.1	<0.001
Diabetes	17 815	36.4	3531	38.2	10 434	35.9	3850	36.5	<0.001
Coronary artery disease	17 535	35.9	3649	39.5	10 054	34.6	3832	36.3	<0.001
Peripheral arterial disease	2317	4.7	405	4.4	1235	4.2	677	6.4	<0.001
Thromboembolism	46 182	94.4	9082	98.3	27 685	95.1	9415	89.1	<0.001
CHA_2DS_2-VASc—continuous (mean, SD)	5.3	1.5	5.4	1.5	5.3	1.5	5.3	1.6	<0.001
CHA_2DS_2-VASc score of 2 or 3	6613	13.5	1041	11.3	3989	13.7	1583	15.0	<0.001
CHA_2DS_2-VASc score of 4 or more	42 288	86.5	8194	88.7	25 114	86.3	8980	85.0	<0.001
Long-term care stays during baseline period									
Cumulative long-term care days (could be non-consecutive), mean (SD)	5.3 (11.2)		7.1 (12.1)		5.0 (10.4)		4.4 (12.1)		<0.001
≥45 long-term care days	745	1.5	167	1.8	396	1.4	182	1.7	0.002
≥90 long-term care days	97	0.20	24	0.26	43	0.15	30	0.28	0.009

*Masked to meet small cell suppression policy.
†Baseline period includes the inpatient-stay adjusted index date and 182 days prior to the index date.
CHA_2DS_2-VASc score, 1 point for congestive heart failure, 1 point for hypertension, 1 point for diabetes mellitus, 2 points for ischaemic stroke/transient ischaemic attack/thromboembolism, 1 point for vascular diseases, 1 point for age 65–74 years, 2 points for age ≥75 years and 1 point for female sex.

Costs of care

Among patients who received ILRs, the total costs of care at baseline (including index date, which means including the costs of the monitor, monitor placement and index hospitalisation) were higher than the other groups (ILR group mean $34 453±$32 357 vs long-term continuous external monitors mean $21 112±$27 850 vs Holter group mean $17 067±$31 266, p<0.001, online supplemental table 11). Mean total costs during 12-month follow-up, which did not include the index date and index hospitalisation, were also higher among patients who received ILRs ($26 967±$42 696) than for long-term continuous external monitors ($24 403±$39 291) and Holter monitors ($22 911±$39 729), p<0.001. Beneficiary out-of-pocket costs related to rhythm monitoring devices paid between the 6-month baseline period and 12 months

Table 2 Adjusted mortality over 12-month follow-up

	Level	HR* (95% CI)
All-cause mortality	ILR	1.00 (0.89 to 1.12)
All-cause mortality	Holter	1.16 (1.05 to 1.28)

The reference group for all models is the long-term external continuous cardiac monitor (>48 hours to 30 days) group.
*Adjusted for CHA_2DS_2-VASc score.
ILR, implantable loop recorder.

following the index date were also higher among patients who received ILRs ($854±$1046) compared with those with long-term continuous external monitors ($64±$174) or Holter monitors ($27±$84), p<0.001.

Risk-adjusted outcomes of ILRs versus external monitors

Mortality

With patients who received long-term continuous external monitors as the reference group, patients who received ILRs had all-cause mortality at 12 months that was not statistically different, HR 1.00 (95% CI 0.89 to 1.12, table 2). Patients who received Holter monitors only had a higher hazard of death, HR 1.16 (95% CI 1.04 to 1.28) compared with those who received long-term continuous external monitors.

Clinical and healthcare utilisation outcomes

With patients who received long-term continuous external monitors as the reference group, in the first 12 months, patients who received ILRs had a higher adjusted odds of a new diagnosis of AF (adjusted OR (aOR) 1.89, 95% CI 1.76 to 2.02) and both new diagnosis of AF and anticoagulant initiation (aOR 2.27, 95% CI 2.09 to 2.48, table 3). In contrast, patients who received Holter monitors had a lower adjusted odds of a new diagnosis of AF and anticoagulant initiation.

The 12-month adjusted odds of haemorrhagic stroke was higher among patients who received ILRs compared with those who received long-term continuous external monitors (aOR 1.60, 95% CI 1.34 to 1.90). Additionally, patients with ILRs were also more likely to have any all-cause acute inpatient hospitalisation (aOR 1.13, 95% CI 1.06 to 1.21).

Costs of care

The adjusted cost ratio (total costs of care PMPM for patients who received ILRs compared with those who received long-term continuous external monitors) was 1.10 (95% CI 1.06 to 1.15, table 4). Medical cost ratios were higher with ILRs, while pharmacy costs were not significantly different. Patients who received Holter monitors had a lower cost ratio compared with those who received long-term continuous external monitors.

Table 3 Adjusted clinical and utilisation outcomes over 12-month follow-up

	Adjusted OR* (95% CI)
Adjusted clinical outcomes over 12 months of follow-up	
Implantable loop recorder	
New atrial fibrillation diagnosis	1.89 (1.76 to 2.02)
New atrial fibrillation diagnosis and anticoagulant initiation	2.27 (2.09 to 2.48)
Haemorrhagic stroke	1.60 (1.34 to 1.93)
Major gastrointestinal bleeding	1.02 (0.91 to 1.14)
Other major bleeding	1.11 (0.84 to 1.46)
Other minor bleeding	1.06 (0.97 to 1.16)
Holter monitor	
New atrial fibrillation diagnosis	0.57 (0.52 to 0.62)
New atrial fibrillation diagnosis and anticoagulant initiation	0.54 (0.48 to 0.62)
Haemorrhagic stroke	0.87 (0.70 to 1.08)
Major gastrointestinal bleeding	1.04 (0.94 to 1.16)
Other major bleeding	0.71 (0.51 to 0.97)
Other minor bleeding	1.10 (1.01 to 1.19)
Adjusted utilisation outcomes over 12 months of follow-up	
Implantable loop recorder	
All-cause acute inpatient	1.13 (1.06 to 1.21)
All-cause emergency department	1.04 (0.99 to 1.10)
Holter monitor	
All-cause acute inpatient	0.99 (0.93 to 1.05)
All-cause emergency department	0.93 (0.88 to 0.98)

The reference group for all models is the long-term external continuous cardiac monitor (>48 hours to 30 days) group.
*All models adjusted for CHA_2DS_2-VASc score.

DISCUSSION

In this study of approximately 49 000 patients who received cardiac monitoring after ischaemic or cryptogenic stroke, we found that ILRs were associated with increased new diagnoses of AF and initiation of oral anticoagulants compared with long-term continuous external monitors. However, there was no reduction in mortality. Given our large sample size and the overall mortality rate of ischaemic stroke due to AF (40% of patients with ischaemic stroke and AF may die within 1 year),[22] if ILR use reduced mortality, this should have been apparent in our data. Costs of care for ILRs, including patient out-of-pocket costs, were significantly higher than for patients who received long-term continuous external monitors.

Our results are consistent with evidence showing that detecting occult AF through screening and initiating oral anticoagulation in patients at increased risk does not improve clinical outcomes. In the LOOP trial, which randomised 6004 patients aged 70–90 with one additional stroke risk factor to ILR versus usual care, the rate of AF detection >6 min in duration was threefold higher in the ILR group and oral anticoagulation was started in 29.1% versus 13.1% of patients, respectively.[13] However,

Table 4 Adjusted per member per month (PMPM) cost outcomes over 12-month follow-up

	Adjusted cost Ratio* (95% CI)
Implantable loop recorder	
Total cost of care, PMPM	1.10 (1.06 to 1.15)
Medical cost, PMPM	1.13 (1.07 to 1.18)
Pharmacy cost, PMPM	1.02 (0.94 to 1.10)
Health plan paid cost, PMPM	1.11 (1.06 to 1.17)
Holter monitor	
Total cost of care, PMPM	0.94 (0.90 to 0.98)
Medical cost, PMPM	0.94 (0.89 to 0.98)
Pharmacy cost, PMPM	0.95 (0.88 to 1.03)
Health plan paid cost, PMPM	0.93 (0.89 to 0.97)

The reference group for all models is the long-term external continuous cardiac monitor (>48 hours to 30 days) group.
*All models adjusted for CHA_2DS_2-VASc score.

neither stroke or systemic embolisation nor major bleeding significantly differed. Similarly, meta-analyses comparing ILR with non-ILR monitoring in three studies among patients with stroke found greater likelihood of AF detection and initiation of oral anticoagulation but no significant decrease in risk of recurrent ischaemic stroke or mortality.[10 12] Our analysis is consistent with these findings of increased likelihood of new AF diagnosis and oral anticoagulation initiation but without improvement in mortality compared with long-term continuous external monitors. Further, the average added cost of ILR use was approximately $13 500 per patient and patients with ILRs had many more outpatient visits than patients with external monitors—some of which were for ILR interrogation, which can be billed as frequently as every 30 days.

There are multiple possible explanations for our findings. First, the clinical significance of ILR detected AF may differ from clinically detected AF.[23] A systematic review and meta-analysis found that AF detected after stroke was associated with a 26% lower risk of recurrent stroke compared with AF known before stroke.[24] As research has shown that subclinical AF is associated with stroke risk,[5] there is a need to define the clinical significance of AF detected on ILRs, particularly short, subclinical episodes of AF.[25]

Second, patients may experience harm after detection of AF, such as bleeding from oral anticoagulants (eg, haemorrhagic stroke) or adverse effects of rhythm control therapy (eg, antiarrhythmic medications) initiated after detection of AF, which mitigate any possible benefits. Given that AF detected by ILRs is nearly always asymptomatic (87% of patients in a study of nearly 700 000 ILR monitoring days never reported AF-related symptoms),[26] if ILRs are not detecting arrhythmias that improve quality of life, it is important that they improve clinical outcomes.

Our findings are somewhat discordant from another observational study that examined ILRs among patients with cryptogenic stroke. Although that study also found increased rate of AF detection and initiation of oral anticoagulation among patients who received ILRs compared with all external cardiac monitors, the investigators found a reduced hazard of death associated with ILRs in a time-to-event analysis.[27] The patients in our study were stratified into two external monitoring categories, with short-term Holter monitors distinguished from long-term continuous external monitors; Holter monitors were associated with a higher hazard of death and so the grouping of external monitors may explain the findings. Further, patients in our study had a higher CHA_2DS_2-VASc score, and there could be heterogeneity of effect based on patient risk for stroke. Finally, the other observational study had suggestion of non-random loss to follow-up of high-risk patients (eg, disabled, hospice and/or long-term care) from the ILR group compared with the control group.

Our findings of lack of reduction in mortality, but increased bleeding and costs, in the context of other published Randomized controlled trial (RCT) evidence finding no clinical outcome benefit from AF screening, suggests that there is a need to reconsider clinical practice guideline recommendations—which are based on AF detection, not on outcomes—for long-term rhythm monitoring to detect AF, since ILRs are increasingly used for that purpose. A recently published RCT that studied oral anticoagulation for device-detected atrial high-rate episodes was stopped early because of safety concerns and futility of efficacy,[14] while another RCT found reduction in stroke or systemic embolism with apixaban compared with aspirin but that was offset by a similarly increased risk of bleeding.[28] Additionally, although ILR placement is generally safe, as ILRs represent an implanted device, they are associated with some complications such as infection, site-related bleeding and pain[29 30] as well as higher costs that are often borne directly by patients. The heterogeneity in rhythm monitoring strategies identified in our study among patients after ischaemic stroke also suggests a lack of clinical consensus as to the optimal rhythm monitoring approach.

Our study should be considered in the context of its limitations. First, as this is an observational study, it is susceptible to unmeasured confounding for variables that could not be matched. As our study represents the best available evidence, it highlights the need for an RCT of secondary prevention use of ILRs. Second, claims data have less reliability in distinguishing new ischaemic stroke from residual signs and symptoms of the original stroke, and so we did not include recurrent ischaemic stroke. Third, it is possible that the criteria for AF diagnosis differed across the monitoring modalities. However, as all three modalities monitor cardiac rhythm, we expect that this was unlikely. Fourth, our study is limited to findings at 1 year. It is possible that differences in mortality could emerge over longer follow-up.

CONCLUSION

Although ILRs were associated with a higher rate of new diagnoses of AF and more initiations of oral anticoagulation compared with long-term continuous external monitors after ischaemic or cryptogenic stroke, there was no reduction in mortality. This finding, along with an increased risk of haemorrhagic stroke and higher costs, raises the possibility of increasing harm caused by the increasing use of ILRs for this indication. These findings raise questions about the benefit of ILRs on clinical outcomes, including mortality, and indicate the urgent need for an RCT to guide clinical practice.

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