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Original Research

Increasing provider awareness of Lp(a) testing for patients at risk for cardiovascular disease: A comparative study

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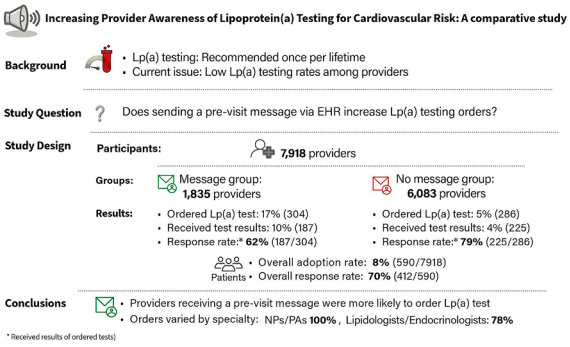
GRAPHICAL ABSTRACT

Increasing Provider Awareness of Lipoprotein(a) Testing for Cardiovascular Risk: A comparative study



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ABSTRACT

Background: Lipoprotein(a) [Lp(a)] is a low-density lipoprotein variant with atherogenic, thrombogenic, and pro-inflammatory properties that may have numerous pathologic effects, including dyslipidemia. Screening for Lp(a) is clinically significant, due to its causal role in atherosclerotic cardiovascular disease (ASCVD). Among clinicians, however, there remains a general lack of both clinical awareness of Lp(a) and adequate tools to track Lp(a) testing in patients.

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lipoprotein(a)
Lp(a)
patient consultation
implementation science
proactive provider messaging

Objective: To study factors affecting Lp(a) screening by: i) determining the effectiveness of messaging providers at a large community health system about Lp(a) screening and measuring the subsequent percentage of Lp(a) tests requested; and ii) by determining the percentage of patients who obtained Lp(a) testing after being advised by the provider.
Methods: From December 2022 through March 2023, messages detailing the need for Lp(a) screening were sent via the Epic EHR™ to providers of patients meeting criteria for Lp(a) testing in advance of scheduled patient appointments. In this prospective study, providers were randomized into 2 groups: those receiving the pre-appointment message (Group 1) and those not receiving the pre-appointment message (Group 2).
Results: Sending pre-appointment messages correlated with more Lp(a) orders (16.6 % v. 4.7 %, $P < 0.001$) and consequently with more tests performed (10.2 % v. 3.7 %, $p < 0.001$). Among provider types, nurse practitioners and physician assistants had the highest number of Lp(a) results per order ($Z = 16.40$, $P < 0.001$), achieving 30.8–39.1 % more test results, even if they did not receive the pre-appointment message. Distribution of Lp(a) values in patients was 59.7 % $\leq$ 29 mg/dL; 9.7 % $>$ 29 and $<$ 50mg/dL; and 30.6 % $\geq$ 50 mg/dL.
Conclusion: Providers who received pre-appointment messages via an EHR were associated with requesting more tests and consequently receiving more Lp(a) results, compared with providers who did not receive messages.

1. Introduction

Lipoprotein(a) [Lp(a)] is a low-density lipoprotein variant produced in the liver and containing apolipoprotein(a). Previous research has shown a direct genetic component of Lp(a) [largely attributed to apolipoprotein(a)], with Lp(a) being considered the most common genetically transmitted dyslipidemia. The genetic component affecting the concentration of Lp(a) has been localized to the LPA gene [1]. This gene generally affects the size of apolipoprotein(a), which is inversely related to the concentration of Lp(a) in the plasma. The combined effect of the size and concentration of apolipoprotein(a) (as determined by the LPA gene), underlies the wide variety of Lp(a) concentrations throughout the population and its variation in different races [2,3]. Due to this genetic component, Lp(a) levels remain relatively stable over a patient's lifetime and therefore may be used for a one-time Lp(a) screening [4].

In recent years, lipoprotein(a) has garnered attention for its potential role as an indicator for cardiovascular risk, in addition to traditional lipid markers [2,3,5]. Lipoprotein(a) is an independent risk factor for cardiovascular disease (CVD), due to its atherogenic and prothrombotic properties [4]. Screening for Lp(a) is important, due to the causal relationship between Lp(a) plasma levels and atherosclerotic cardiovascular disease (ASCVD) [6]. Thus, testing is indicated for individuals at high risk for developing CVD, including those with a personal or family history of premature ASCVD (before age 55 in males or age 60 in females); severe hypercholesterolemia (LDL $\geq$190 mg/dL); familial hypercholesterolemia; and/or or calcific aortic valve stenosis [4,7–9]. Between 2018 and 2022 Lp(a) measurement was added to the clinical guidelines of 5 prominent organizations [2,3,6,10,11]. Recent National Lipid Association (NLA) guidelines advise Lp(a) testing for all adults aged 18 years and older. (This update occurred after our study was conducted) [2,3].

Despite evidence that elevated Lp(a) levels are linked to cardiovascular morbidity and mortality, there are barriers to ordering Lp(a) screening, including: lack of awareness among providers of its significance and overall implications for cardiovascular health [12]; lack of reimbursement for the test; absence of FDA-approved treatment options with established benefits for vascular outcomes; and non-availability or lack of resources for the Lp(a) test [13,14]. The gap in treatment options has led to a focus on developing new drug therapies. Currently, there are medications with promising results in the clinical trial pipeline. This reinforces further the importance of Lp(a) screening [15–20].

This study aimed to increase both physicians' and patients' awareness of Lp(a) by determining if proactive communication with providers about Lp(a) screening is effective, and by measuring the percentage of patients who obtained Lp(a) testing. We also determined the distribution of Lp(a) results among those who were tested, to identify potential pathways for improving Lp(a) awareness, screening, and identification of patients who may benefit from additional cardiovascular risk-reduction strategies.

2. Methods

This prospective, randomized trial of 7918 patients took place in a large community health system in northern Kentucky and southeastern Indiana, between December 2022 and March 2023. The study was approved by the St. Elizabeth Health Care Institutional Review Board and a waiver for informed consent was approved. From our institution's lipid registry (established in 2020) [21–24] and utilizing 2217,562 de-identified records in the Epic EHR™, approximately 45,000 individuals met the National Lipid Association (NLA) guidelines for Lp(a) testing. Of these, 7918 (18 %) were enrolled based on the inclusion criteria (Table 1, Fig. 1), including personal or family history of premature ASCVD; severe or familial hypercholesterolemia; calcific aortic valve stenosis and scheduled appointment with a specialty provider in the next six months.

Sample size was based on the availability of patients meeting the inclusion criteria with the understanding that sample sizes in the thousands are ideal to achieve reasonable statistical power for proportion methods associated with binary variables. We used a 1:1 computer-generated randomization scheme to match patients based on gender, age

Table 1
Inclusion and exclusion criteria.

Inclusion Criteria	Definition
Personal or family history of ASCVD	Before age 55 in males or age 60 in females with EHR record of: • implantable cardiac defibrillator • angina pectoris • acute myocardial infarction • ST or non-ST-elevated myocardial infarction • myocardial infarction complications • acute or chronic ischemic heart disease • cerebral infarction • arterial embolus thrombosis or atheroembolism
Familial hypercholesterolemia [25]	Dutch Lipid Clinic Network (DLCN) score $\geq$ 6 or meeting American Heart Association criteria[23]
Severe hypercholesterolemia	LDL $\geq$190 mg/dL
Calcific aortic valve stenosis [26]	
No previously recorded Lp(a) result	
Scheduled appointment in the next 6 months with: physician, nurse practitioner, physician's assistant, or pharmacist in selected specialties	• cardiology • family medicine • internal medicine • endocrinology • medication management
Exclusion criterion	
Previous Lp(a) result documented in patient's EHR	

group, and Dutch Lipid Clinic Network (DLCN) score. There was no blinding for this prospective study.

Providers were randomized into 2 groups: either to receive (Group 1) or not receive (Group 2) a pre-appointment message. Due to time constraints, this method was not fully implemented and thus required an unplanned change to the protocol. Consequently, only one-half (n = 1835) of Group 1 providers were sent the message, resulting in an approximate 1:3 pseudo-randomization. Despite pseudo-randomization, demographic balance between the groups remained intact.

Providers in Group 1 were sent a standardized staff message via Epic approximately one week prior to the patient's scheduled appointment (Fig. 2). The subject line, "Lp(a) evaluation – lab needed" generated a report to document the message was sent. For this iteration of the study, we did not field test the message with physicians and did not document whether the message was read. Because no pre-appointment message was sent to providers in Group 2, we used the lipid registry database to determine if an Lp(a) test was ordered and /or resulted for patients in both groups.

Data for both groups were collected from the Epic reports after the patient visit. Subjects were de-identified and statistical analyses were performed by the Northern Kentucky University Burkardt Center (a statistical collaboration center). The pre-specified primary outcome measure was the ordering of a Lp(a) laboratory test (a binary yes/no variable). Secondary outcomes included: receiving the Lp(a) lab test result (yes/no); the numeric value of that result; and the potential relationship between coronary artery disease (CAD) and the test result. Descriptive summary statistics include counts and percentages to summarize categorical variables, while means and standard deviations summarize quantitative variables. Both the primary outcome, 'requested Lp(a),' as well as the secondary outcome, 'resulted Lp(a),' were analyzed for between-group differences using Z-tests and confidence intervals for proportions. Further outcomes were examined using Chi-square tests,

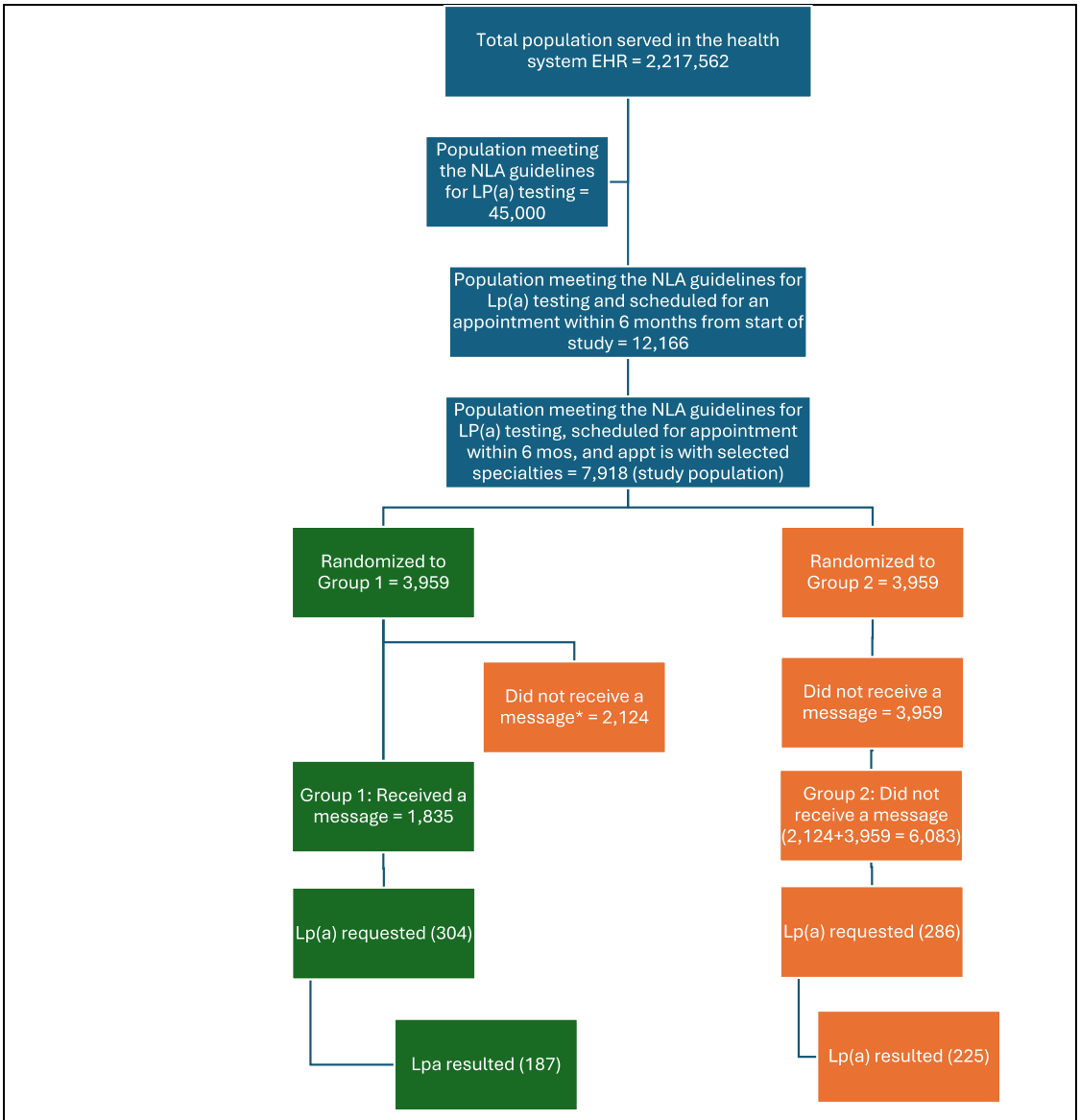

Fig. 1. Distribution of patients meeting Lp(a) testing criteria in a healthcare population in northern Kentucky.

Hello {DR/MS/MR}

{Ms/Mr} has been identified as meeting criteria to have a lipoprotein(a) [Lp(a)] test. Elevated Lp(a) has been identified as a risk factor for development of cardiovascular disease due to its atherogenic and prothrombotic properties. Patients who have a personal/family history of CAD, a diagnosis of familial hypercholesterolemia, ever had a LDL ≥190, and/or calcific aortic valve narrowing are indicated for Lp(a) testing.

This patient has an upcoming appointment with you on *

A one-time Lp(a) screening assessment can be done to help risk stratify your patient for future cardiovascular complications. This assessment is done via a blood draw that does not require fasting. Testing can be performed standalone or in addition to concurrent blood draw orders. This test for this patient can be {added to the lab the patient had done within the previous 2 days; can be ordered with labs scheduled to be done within the next 7 days; or can be ordered prior to or at the appointment as there are no labs currently ordered}. This lab test is inexpensive and typically covered by insurance plans. The lab order can be found under Lipoprotein (a) (aka LPA).

If the Lp(a) comes back within normal limits, no further intervention is needed. If the test comes back elevated, you may want to share the patient-friendly education document found here:

https://www.lipid.org/sites/default/files/elevated_lipoprotein_a.pdf

Thank you for your participation,

The Cardiometabolic Risk Reduction Research Team

Fig. 2. Standardized provider staff message.

Mann-Whitney test (specifically for Lp(a) levels), and logistic regression analysis.

3. Results

Forty-five thousand patients (2 %) of the St. Elizabeth healthcare population met the criteria for Lp(a) testing [5,7] of these, 7918 patients were enrolled. Table 2 shows the distribution of Lp(a) values for the enrolled population. It is grouped by: the presence or absence of known ASCVD; whether or not Lp(a) was tested; and Lp(a) test results, when available.

Table 3 shows the distribution of Lp(a) results for the total population and when grouped by the presence or absence of ASCVD (Figure S1).

Table 4 shows the number of Lp(a) tests ordered and the number of test results returned in both Groups 1 and 2. Group 1 (message sent) showed a 10.1–13.6 % greater likelihood of ordering the Lp(a) lab ($P < 0.001$, Table 4) and were 5–8 % more likely to receive test results ($P <$

Table 2
Distribution of Lp(a) levels for the total study population and for those with ASCVD.

Group		Lp(a) Tested					Lp(a) Not tested
		Total Lp(a) tested	Lp(a) ≤29	Lp(a) >29	Lp(a) >29 or < 50	Lp(a) ≥50	
Total population	7918	412	246	166	40	126	7506
		(*5.2 %)	(*3.1 %)	(*2.1 %)	(*0.5 %)	(*1.6 %)	(*95 %)
		(†100 %)	(†59.7 %)	(†40.3 %)	(†9.7 %)	(†30.6 %)	
ASCVD	2623 (33 %)	192	108	84	16	68	2431
		(*2.4 %)	(*1.3 %)	(*1.1 %)	(*0.2 %)	(*0.9 %)	(*30.7 %)
		(†46.6 %)	(†26.2 %)	(†20.4 %)	(†3.9 %)	(†16.5 %)	(†92.7 %)
		(‡7.3 %)	(‡4.1 %)	(‡3.2 %)	(‡0.6 %)	(‡2.6 %)	
		(§100 %)	(§56.3 %)	(§43.8 %)	(§8.3 %)	(§35.4 %)	
No ASCVD	5295 (67 %)	220	138	82	24	58	5075
		(*2.8 %)	(*1.7 %)	(*1.0 %)	(*0.3 %)	(*0.7 %)	(*64.1 %)
		(†53.4 %)	(†33.5 %)	(†19.9 %)	(†5.8 %)	(†14.1 %)	(†95.8 %)
		(‡4.2 %)	(‡2.6 %)	(‡1.5 %)	(‡0.5 %)	(‡1.1 %)	
		(§100 %)	(§62.7 %)	(§37.3 %)	(§10.9 %)	(§26.4 %)	

* % of patients tested for Lp(a) per total population enrolled.
† % of patients tested for Lp(a) per total tested for Lp(a).
‡ % of patient tested for Lp(a), per subgroup (ASCVD or not).
§ % of patient tested for Lp(a), per subgroup (ASCVD or not) AND tested for Lp(a).

Table 3
Lp(a) results for total study population and when grouped for ASCVD.

Variable Lp(a)	N	Mean	StDev	Min	Q1	Median	Q3	Max
Total study population	412	44.87	53.93	2.00	6.00	19.50	71.00	293.00
ASCVD								
Yes	192	52.59	59.72	2.00	6.25	21.0	80.00	293.00
No	220	38.39	47.52	2.00	6.00	17.0	54.75	240.00

Table 4
Lp(a) ordered and resulted in Groups 1 and 2.

	Lp(a) Ordered		Lp(a) Resulted	
	Group 1 (Message)	Group 2 (No Message)	Group 1 (Message)	Group 2 (No Message)
Sample Size	1835	6083	1835	6083
Event	304	286	187	225
Sample percent	0.166	0.047	0.102	0.037
95 % CI for percent	(0.149, 0.183)	(0.042, 0.053)	(0.088, 0.117)	(0.032, 0.042)
Sample Difference	0.119		0.0649	
95 % CI for Difference	(0.101, 0.136)		(0.050, 0.080)	
Z-Value	13.05		8.70	
P	<0.001		<0.001	

0.001, Table 4).

Despite more test orders and results occurring in Group 1, significantly more tests (as a percentage of those ordered) were completed by patients in Group 2 ($P < 0.001$, Table 5) and providers in Group 2 who ordered the test had an estimated 9.9–24.4 % higher result rate.

Table 5
Lp(a) ordered vs Lp(a) resulted in Groups 1 and 2.

	Group 1 (message)	Group 2 (no message)
Lp(a) ordered	304	286
Lp(a) results obtained	187	225
Percent of resulted Lp(a)	0.615	0.787
95 % CI for percent resulted Lp(a)	(0.558, 0.670)	(0.735, 0.833)
Percent sample difference	0.172	
95 % CI for difference	(0.099, 0.244)	
Z-value	4.64	
P	<0.001	

3.1. Lp(a) orders and results among specialty providers

To analyze this paradox, we cross referenced the results (Table 4) by adjusting for the requesting provider's specialty. Importantly, randomization of Groups 1 and 2 did not account for the specialty of the provider receiving the message or ordering the test. Fig. 3 shows Lp(a) results based on the specialty group. Nurse practitioners/physician assistants achieved the highest number of results per order ($Z = 16.40$, $P < 0.001$), having 30.8–39.1 % more results compared with other specialties (Fig. 3). This was followed by endocrinologists, with 15–30 % more results compared with internal/family medicine providers ($Z = 5.54$, $P < 0.001$). There was no evidence of a difference between cardiovascular and internal/family medicine specialties ($Z = 1.14$, $P = 0.253$) (Fig. 3, Table S1, Figure S2a, S2b).

3.2. Impact of messaging among specialty providers

Fig. 4 shows results based on the specialty group and whether or not the provider was sent a pre-visit message. Nurse practitioners and physician assistants obtained an Lp(a) result for every test ordered, regardless of whether a pre-visit message was or was not sent (Fig. 4). There also is evidence that other specialty groups who were not sent the pre-visit message may have obtained more Lp(a) results compared with those who were sent the message, but this did not reach statistical significance [(cardiology: ($Z = -1.37$, $P = 0.170$); internal/family medicine: ($Z = -1.35$, $P = 0.178$)]. Among endocrinologists who were not sent the pre-visit message, 87 % obtained more Lp(a) test results, compared with those who were sent a message ($Z = -4.08$, $P < 0.001$).

3.3. Comparing Lp(a) values among study groups

There was no significant difference in the Lp(a) values between the study groups ($P = 0.725$) (Fig. 5).

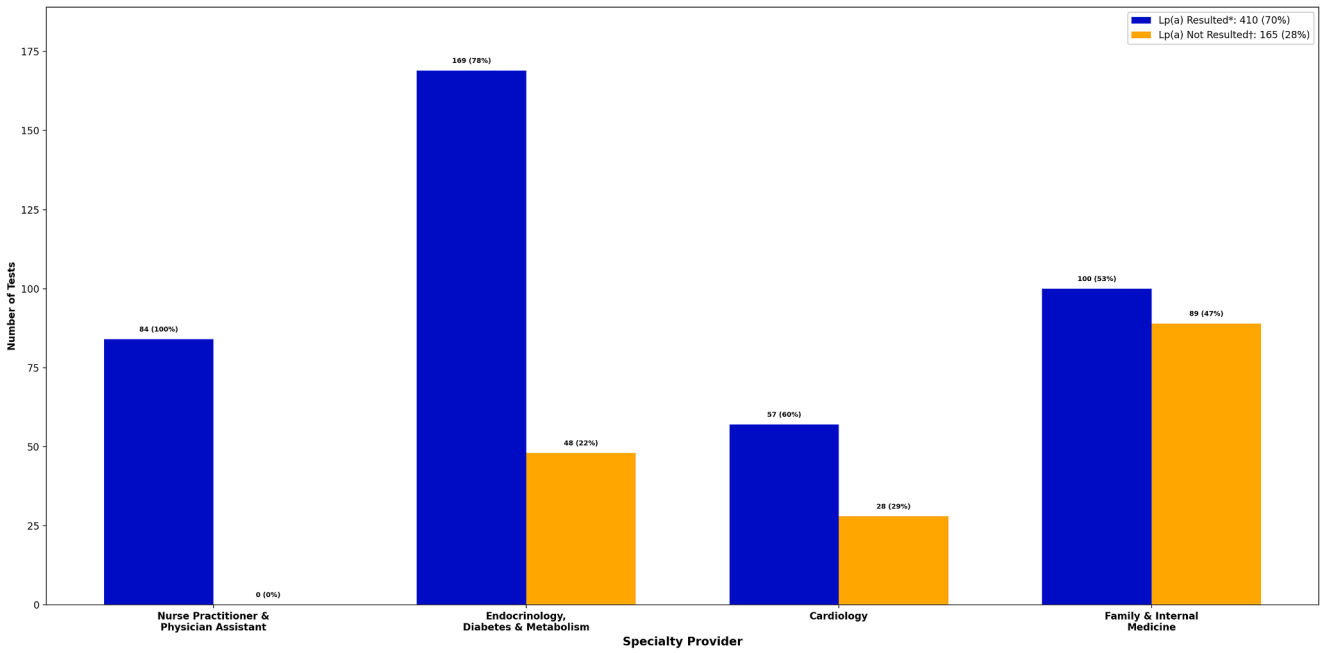

Fig. 3. Lp(a) Tests requested by specialty provider ($n = 585$).
* 2 patients did not have specialty of provider recorded in the EHR, †Test ordered by provider, but not completed by patient

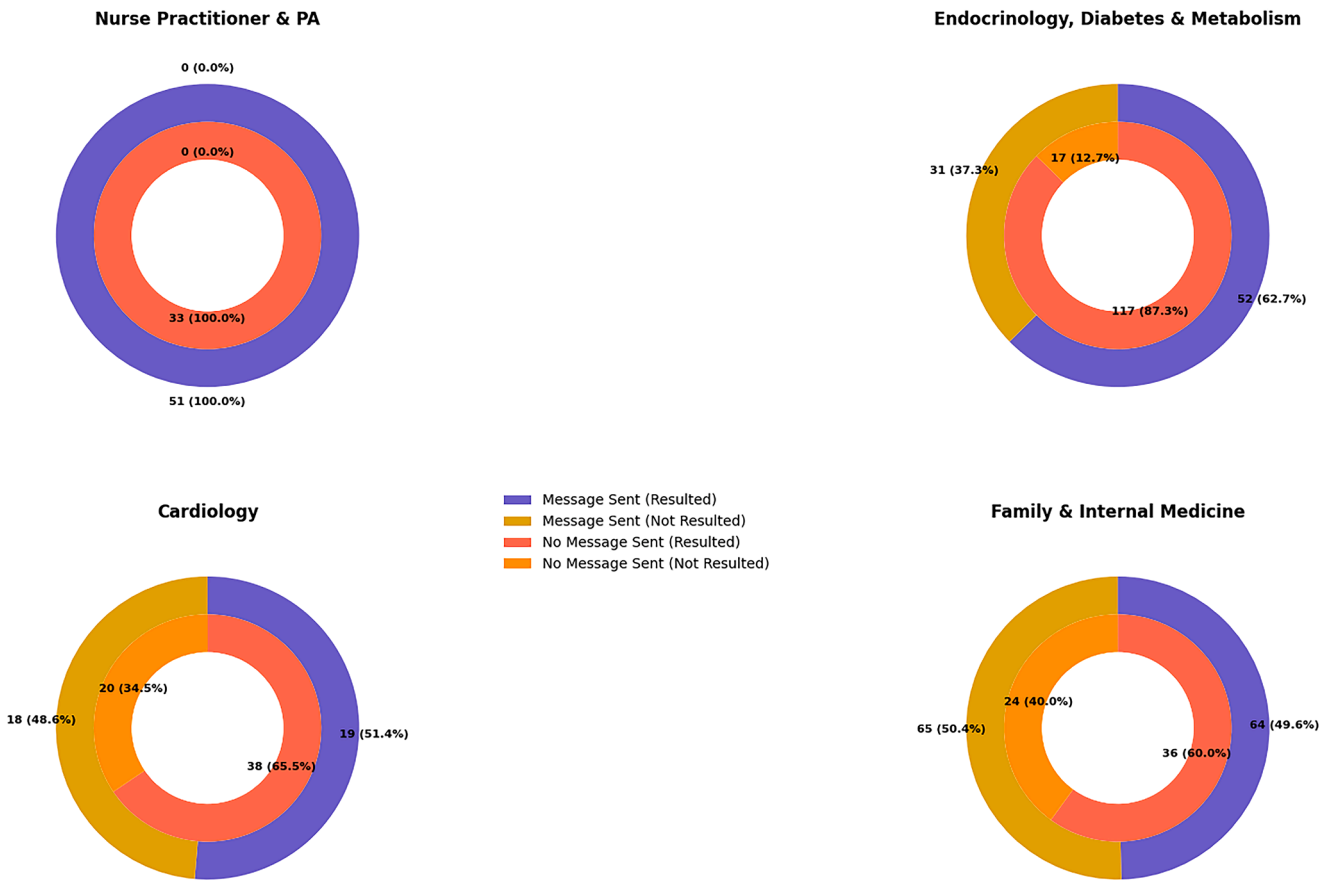

Fig. 4. Lp(a) Results by specialty provider and whether message sent or not.

3.4. *Comparing Lp(a) values among different comorbidities*

A pooled analysis of Lp(a) results from both Groups 1 and 2 revealed a significant increase in median Lp(a) levels exclusively in individuals with coronary artery disease (CAD) ($P = 0.023$), compared with those without CAD. Notably, this difference was not observed among individuals with other comorbidities, including diabetes (DM), hypertension (HTN), obesity, or those with varying levels of HCC scores (Fig. 6).

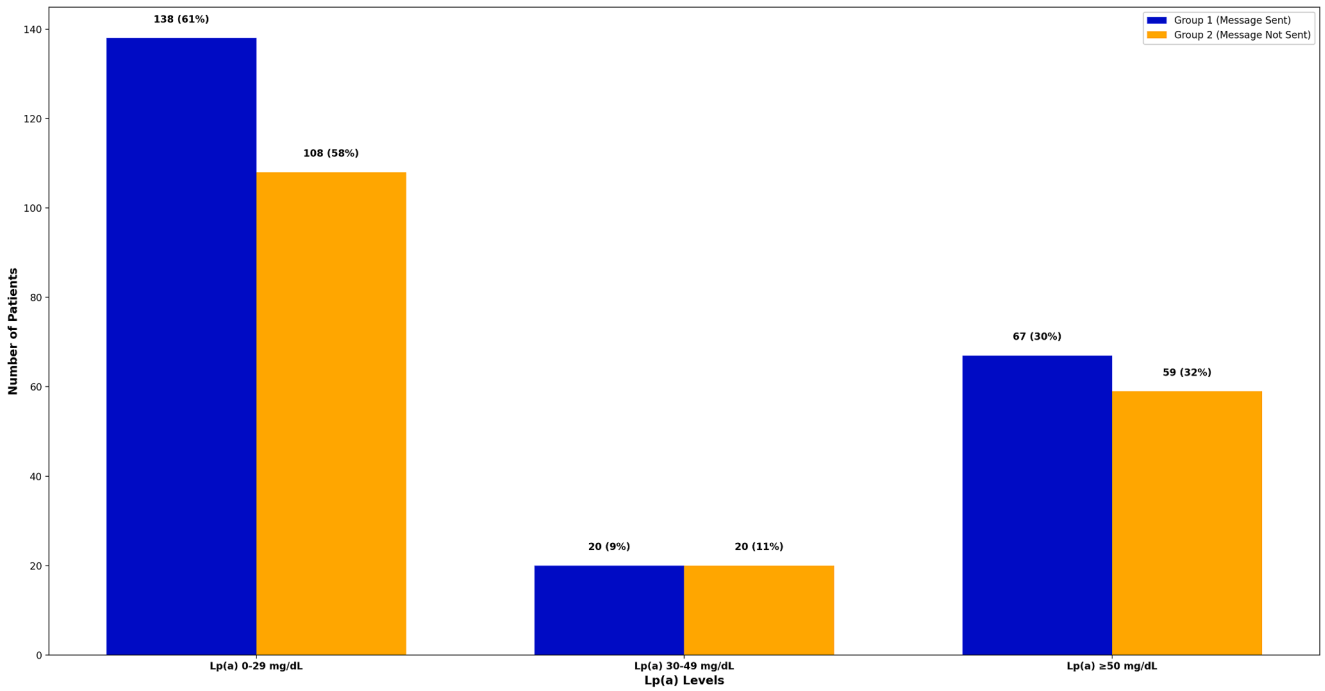

Fig. 5. Lp(a) Results by Lp(a) level and study group.

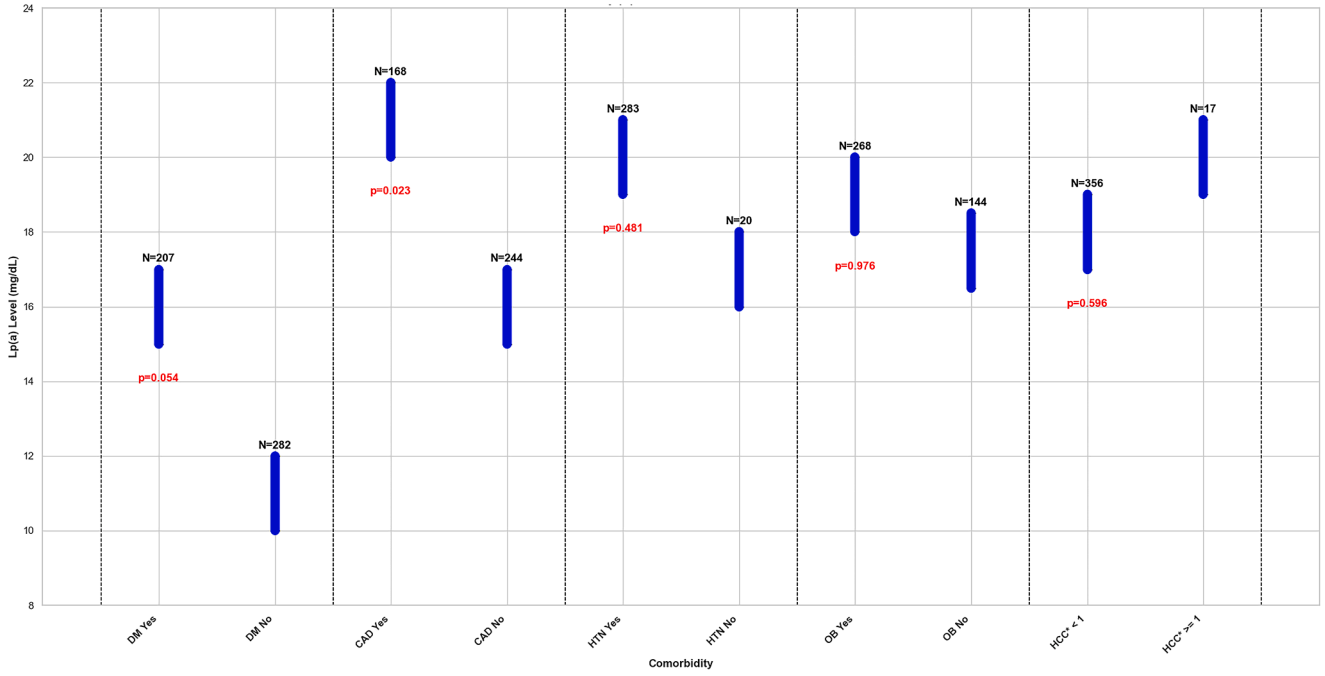

Fig. 6. Median Lp(a) in different studied comorbidities.
* Hierarchical Condition Category (HCC) score is used in health care to assess the severity of a patient's health status and to predict future healthcare costs. HCC scores help adjust payments based on the health status and expected resource needs of individuals, particularly within Medicare and other risk-adjustment programs.

Our study was not adequately powered to assess the impact of Lp(a) on CAD.

4. Discussion

Lipoprotein(a) is a well-established, independent, continuous causal risk factor for ASCVD [6,8,23,27]. Guidelines from the National Lipid Association (NLA)[7] others [4,7,28] recommend measuring Lp(a) in individuals who have various clinical diagnoses and the 2024 NLA updates recommend measuring Lp(a) once in every person's lifetime, regardless of family history [2,3,6,10,11]. The NLA guidelines also acknowledge a need for educational materials to increase Lp(a) awareness among clinicians, patients, and other stakeholders [2].

Our investigation adhered primarily to previous NLA recommendations outlined by Wilson, Jacobson et al. in 20,19[7] and 20,22[5] to identify patients eligible for Lp(a) testing, and corroborates other studies regarding the importance of early, proactive identification of those with a high Lp(a) in order to manage CVD risk [14,23,29]. To date, there is a

low adoption rate for ordering Lp(a) testing and most patients requiring the test do not receive it through specialty or routine clinical care, except through an intervention program [27,30]. For example, only 0.3 % of more than 112 million individuals screened or treated for ASCVD between 2012 and 2019 in the US Family Heart Foundation integrated dataset, were tested for Lp(a) [31]. In our study, only 17 % (7918) of the 45,000 who qualified for Lp(a) testing were scheduled for an upcoming clinical care appointment with a specialist provider, while the remaining (83 %) did not have an upcoming opportunity for testing in the near future. There also was only a 17 % response rate (304 of 1835, Table 4) for test orders from providers receiving the message; a 5 % response rate (286 of 6083, Table 4) from providers who were not sent the message, and an 8 % adoption rate for tests orders for the entire enrolled patient population.

Of patients enrolled in our study, 33 % had known ASCVD, but none had the test prior to enrollment. Of the 8 % for whom the test was requested, 412 (5 % of total enrolled), 70 % underwent Lp(a) testing, whereas 177 (30 %) did not have the test done, despite being advised. Failure to have testing done despite being advised might reflect some of the barriers suggested by other studies, including a lack of awareness and perceived lack of clinical value both by providers and patients, providers' continued perception of limited reimbursement for the test, and a lack of robust clinical decision support tools to help address the gap in knowledge [2,27,30].

Of the 33 % of patients in our study with ASCVD, only 7 % completed Lp(a) testing. This is comparable to the 5 % completion rate found by Wilkinson et al., of 2710 participants with calcific aortic stenosis [26]. In the Lp(a) HERITAGE [14] study, 14 % of patients had historical data of Lp(a) prior to the study start and the remainder (86 %) had the test after enrollment. Most programs established for proactively identifying Lp(a) [14,32,33] recruited patients with a history of ASCVD to improve management of secondary prevention. We found a notable increase in median Lp(a) levels (Fig. 6) when compared with individuals without diagnosed CAD. The mean Lp(a) concentration was 52 mg/dL in subjects with CAD (Table 3), which aligns with other research showing Lp(a) levels above 50 mg/dL as an independent predictor for CAD [31].

It is important not to limit Lp(a) testing only to those with known ASCVD, given the importance of CVD primary prevention, including lifestyle modification, pharmacologic intervention, and cascade screening for elevated Lp(a) [5,25,27,31,34,35]. In our study, for example, 47 % of patients tested for Lp(a) had known ASCVD (Table 2) which is higher than the 31 % reported by McGown et al. [31]. It is unknown whether or not the 14 % of patients with no known ASCVD but clinically significantly elevated Lp(a) (Table 2) had undiagnosed ASCVD. This is particularly important, since some patients in our study ($n = 6$, Figure S1) did not yet have known CVD, but had an Lp(a) >180 mg/dL (a risk equivalent to those with FH[36]) and consequently required aggressive treatment intervention.

Notably, in the subset of patients with evidence of ASCVD ($n = 2623$, 33 %), 44 % had Lp(a) levels >29 mg/dL and 35 % > 50 mg/dL (Table 2). These percentages were higher than those reported in the Lp(a) HERITAGE study by Nissen et al. [14], in which 38 % had Lp(a) >29 mg/dL and 28 % had levels >50 mg/dL. It might be possible that our population has a higher prevalence of elevated Lp(a) levels compared with other populations, which might contribute partially to the higher prevalence of CVD compared with the rest of the USA [2]. These findings align with the Lp(a) HERITAGE study that showed a trend among patients with ASCVD: a higher percentage of those with Lp(a) >50 than those with Lp(a) >29, but lower than 50 mg/dL (Tables 2 and 3). In addition, 40 % and 31 % of patients in our study showed elevated Lp(a) levels exceeding 29 mg/dL and 50 mg/dL, respectively (Fig. 3). This is similar to the prevalence reported in a previous US-based study at a tertiary referral center involving 915 patients [37]. These figures are slightly higher than figures in the NLA 2019 scientific statement [7,37] and may be due to the focused inclusion criteria for our study, including patients that may have a higher chance of having an elevated Lp(a) with CVD.

4.1. Messaging

The messages sent in this study served two main purposes: i) to motivate providers to order the Lp(a) test and ii) to increase their awareness of the test's importance [5,14,27]. Our results show that sending pre-appointment messages via the EHR to providers with patients at high risk for having an elevated Lp(a) (Group 1), was associated with a higher number of provider orders for Lp(a) testing (17 %) and consequently a higher number of Lp(a) results (10 %), compared with providers who were not sent a message (Group 2) ($P < 0.001$) (Table 4). In the Lp(a)HERITAGE study, 86 % of Lp(a) testing occurred after patients were enrolled into the study. This is due to the difference in study design: the HERITAGE study used active patient recruitment at research centers, whereas our study incorporated an existing clinical EHR framework to integrate Lp(a) messaging into routine, ongoing clinical care.

Paradoxically, our study showed a statistically higher percentage of patients having the Lp(a) test done (with results) among providers who were not sent the staff message (Group 2), compared with providers who were sent the message (Group 1) (Table 5). We found this was associated primarily with provider specialty: with nurse practitioners and physician assistants, followed by endocrinologists receiving more results for orders sent; followed by cardiology and internal medicine/family medicine providers (Fig. 3). Results showed that more Lp(a) results were obtained by endocrinologists who did not receive the EHR message (Fig. 4). This is mostly likely due to the longstanding lipid clinic hosted by St. Elizabeth Healthcare [21] and staffed by lipid specialists [38], clinical pharmacists, and a dietitian. This clinic has been a referral hub for patients with FH [23] and is adopting the same concept for the Lp(a) clinic [29,39–41]. This corroborates other studies, such as Eidensohn et al. review of EHR records from their center's lipid clinic showing increases in Lp(a) testing over the study period [41]. Further exploration of the distribution of providers ordering Lp(a) is available in the supplemental material.

5. Study limitations

Although this study was completed prior to release of the updated NLA guidelines [2], the guidelines suggest that until Lp(a) testing becomes widespread, it is reasonable to incorporate it into order sets for specific conditions, as we have done in our study. [2] We were not able to undertake a full demographic characterization for our study population, as other studies have [14,41] but we estimate that most patients recruited into our study were from the northern KY area where there is a high prevalence of CVD. Kentucky is ranked as having the 8th highest mortality rate from cardiovascular disease in the country and heart disease is the leading cause of death in this state [2]. The unplanned protocol change, and lack of blinding may have introduced biases to this study. This study highlights the challenges of implementing randomized interventions in clinical settings, but still supports the generalizability of its findings, particularly given the large sample size ($n = 7918$), which provides robust data for statistical analysis despite protocol modifications. Not all providers read EHR staff messages (especially messages sent by medical students) and we did not record whether or not the sent messages were read, and we did not test the effectiveness or readability of the message content. In addition, we did not evaluate the modification of CVD risk awareness (among patients and providers), or management in patients with high Lp(a), (including lifestyle changes or lipid lowering therapies). Lastly, the Lp(a) assay at our hospital uses mg/dL, which is sensitive to the size of the apo(a) isoform and may report values that deviate from the real concentration [4,27].

6. Strengths

This study establishes a platform for identifying patients who qualify for Lp(a) testing (based on previous and current NLA guidelines[5]) that can be incorporated into existing clinical workflows [27,42]. The EHR-based intervention and its integration into clinical workflows facilitate understanding of real-world implications for practice. It is not limited only to patients with known ASCVD; therefore, primary and secondary CVD risk management strategies can be optimized for patients with a high Lp(a). Our study included stakeholder providers in both primary care and specialty service lines (cardiology, endocrinology, and/or lipidology), including physicians, physician assistants, and advanced nurse practitioners. This meets the 'sustainable program' requirements identified by Schubert, et al., in which buy-in from multi-level stakeholders, cost effectiveness, and sufficient human resources are needed to support successful screening initiatives [43].

7. Conclusion

To our knowledge, this is the first prospective, randomized study that leverages electronic health records (EHR) to proactively identify qualified patients and to target pre-appointment messages to healthcare providers prompting them to include Lp(a) testing in their regular care routine. This proactive intervention may be useful in heightening awareness, especially since it now can be automated in an EMR. The study highlights the importance of Lp(a) screening for primary and secondary CVD prevention and is the first study to incorporate Lp(a) screening into an existing clinical workflow (EHR) in a prospective, randomized manner, among a variety of provider types, to support future primary and secondary CVD prevention. Sending messages to select providers was associated with more tests ordered and consequently more Lp(a) results received, compared with providers who were not sent messages. However, results also revealed important trends among and within specialty providers that will be useful in targeting future message design, delivery, and incorporation into clinical workflow. We found a differential pattern within each specialty: a minority of providers ordered the majority of Lp(a) tests, and a variable number received results. This reflects the diverse scope of interest in lipidology within specialty groups, further reinforcing the importance of Lp(a) screening and revealing future opportunities for workflow innovation to increase testing.

Author agreement

All authors have participated in this research and/or article preparation. All authors have approved the final article and supplementary information.

All authors agree to be accountable for all aspects of the work related to the accuracy or integrity of any part of the work.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2024.100895.

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