Eko
Low Ejection Fraction Tool (ELEFT)

User Manual

Version - V7.4.0
English

1.1 Overview

This manual is intended to provide information to guide trained operators in the safe and effective operation of the Eko Low Ejection Fraction Tool. It is important that you read and understand all instructions in this manual before operating the device, and pay careful attention to the warnings and cautions throughout the manual. The term “low ejection fraction”, as used throughout this manual, refers specifically to a reduced ejection fraction of ≤ 40%.

CAUTION: Eko Low Ejection Fraction Tool is for prescription use only (Rx). Federal (USA) law restricts this software to sale to or on the order of a clinician.

Eko Health, Inc. assumes no responsibility for any injury to anyone, or improper use of the product, that may result from failure to use this product in accordance with the instructions, cautions, warnings, or statement of intended use published in this manual.

Eko Health, Inc. may have patents, patent applications, trademarks, copyrights, or other intellectual property (IP) rights covering subject matter in this document. The use of this document does not give anyone license to these patents, trademarks, copyrights, or other intellectual property.

The lifetime of the device (ELEFT) is 2 years.

1.2 Notices

For general and product related comments, questions, or concerns, please contact Eko directly.

Serious Incident Reporting For the EU Market:

If a serious incident has occurred in relation to the device, it should be reported to the manufacturer and the competent authority of the Member State in which the user and/or patient is established. A serious incident means any incident that directly or indirectly led, might have led or, in case of recurrence, could lead to any of the following: the death of a patient, user or other person, the temporary or permanent serious deterioration of a patient’s, user’s, fetus or other person’s state of health, or a serious public health threat.

Manufacturer:
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Product Reference and Information
ekohealth.com/ifu

Patents
Listing of applicable U.S. Patents in compliance with 35 U.S.C. §287:
ekohealth.com/patents

Disclaimer
The information contained in this document is subject to change without notice.

1.3
Safety Related Labels & Symbols

Consult electronic instructions for use
http://www.ekohealth.com/ifu

Catalogue Number

Manufacturer

Caution

Medical Device

Unique Device Identifier

1.4
Cautions

- **The Eko Low Ejection Low Ejection Fraction Tool (ELEFT) output is NOT a diagnosis.** Findings from the ELEFT are only meaningful in conjunction with clinician over-read and interpretation. The user should not rely on the lack of a suspected finding to rule out follow-up and device output should not replace a full clinical evaluation of the patients.
- ELEFT can provide automatic computer interpretations. A computer-generated interpretation cannot replace sound medical reasoning by a trained professional. Therefore, a physician should always review the interpretation and final analysis should always be obtained by a physician. Proper administration, diagnosis and implementation of the test is the physician's responsibility.
- The quality of the interpretations depends heavily upon the quality of the inputted data.
- The medical history and physical examination results must be taken into consideration during the decision-making process.
- The software should not be used on patients where the physician has difficulty using an electronic stethoscope.
- ELEFT has only been evaluated for the detection of a left ventricular ejection fraction (EF) of less than or equal to 40%. It cannot detect heart attacks. It is not intended for life-supporting or life-saving functionality.
- Medication adjustments should not be made based on these outputs.
- The ELEFT may be unable to return a result if the Eko stethoscope is unable to connect to the mobile device over Bluetooth or if the mobile device is unable to connect to the internet.
- The ELEFT algorithm may generate false positives and many of these false positives can be due to cardiovascular comorbidities (e.g. Left bundle branch block or Permanent Atrial Fibrillation) that are known to cause marked variations in ECG appearance.
- In the case of a positive result, consider referral for cardiology consult or echocardiogram, which can confirm the presence or absence of Low Ejection Fraction.
- ELEFT is intended for use in patients who are at-risk for heart failure.
- ELEFT should not be used in lieu of an echocardiogram or other diagnostic tests.
- ELEFT should not be used to monitor disease progression.

1.5
Indications for Use

Eko Low Ejection Fraction Tool (ELEFT) is a software intended to aid clinicians in identifying individuals with Left Ventricular Ejection Fraction (LVEF) less than or equal to 40%. ELEFT takes as input ECG and heart sounds and is intended for use on patients at risk for heart failure. This population includes, but is not limited to, patients with: coronary artery disease; diabetes mellitus; cardiomyopathy; hypertension; and obesity.

The interpretations of heart sounds and ECG offered by the software are meant only to assist healthcare providers in assessing Left Ventricular Ejection Fraction ≤ 40%, who may use the results in conjunction with their own evaluation and clinical judgment. It is not a diagnosis and should not be used for monitoring patients diagnosed with heart failure. This software is for use on adults (18 years and older).

1.6
Clinical Benefits

Eko Low Ejection Fraction Tool (ELEFT) is a non-invasive heart failure screening tool that is able to identify low ejection fraction with the same or better sensitivity and specificity than any other currently available screening method. Visualizing ELEFT outputs greatly increases the probability of a clinician diagnosing heart failure in patients at risk for heart failure, with the intention of improving patient outcomes.

1.7
System Network

This manual provides instructions for the use of the Eko Low Ejection Fraction Tool. It is assumed that the user is familiar with basic mobile application use on mobile and desktop devices.

It is highly recommended that users of the mobile app use device and networking security features to protect patient data created and stored using this software, in addition to security features embedded in the system.

The Eko Low Ejection Fraction Tool requires a minimum internet connection speed. The recommended upload speed for the mobile app is 4000 Kbps. 4G cellular data service or similar is recommended.

LOW EF DETECTION

The Low EF detection analysis identifies possible depressed left ventricular EF of 40% or less. It is not a diagnosis; it is only a potential finding. You should conduct further evaluation if a low EF is detected. **It will not detect cardiac conditions that do not cause low EF.** A low EF finding is often a recommendation for echocardiography or specialist referral.

The device is solely intended to analyze heart sound (PCG) and ECG recordings collected by healthcare professionals or other operators with at least 5 years experience in collecting clinical data. However, data analysis/interpretation is restricted to qualified medical professionals.

Proper handling of the stethoscope to minimize external background noises and hand rub/clicks should be practiced. This software cannot analyze lung sounds.

The possible results are:

- Poor ECG Signal
- Normal Ejection Fraction Detected
- Reduced Ejection Fraction Detected

Please note that ELEFT uses signal quality classifier algorithms to determine whether the ECG and PCG recordings are of sufficient signal quality for the ELEFT analysis. If a recording has poor ECG, the interpretation will return with a result of *"Poor ECG signal"* and will not analyze the recording.

If a recording has poor heart sound signal quality, the following message is shown to the user - *"Due to poor signal quality, heart sounds were excluded from the analysis. Consider repeating the test for an analysis which includes both ECG and heart sounds."*

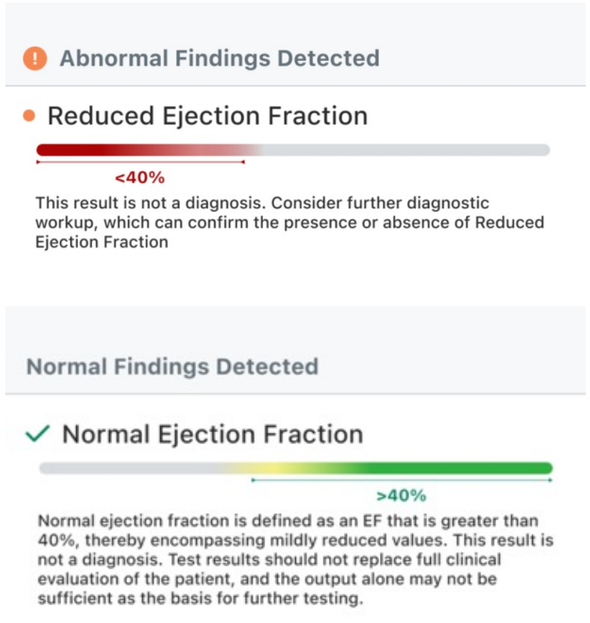
The performance of the signal quality classifier algorithms have been validated and the results are provided in Table 1 below.

Table 1: Performance metrics for the signal quality classifier algorithms

Good Signal	Prevalence (%)		Sensitivity (%)	
	Actual	**Min Req**	**Actual**	**Min Req**
Good PCG Signal	87.8 (95% CI: 86.0– 89.4)	75.0	94.8 (95% CI: 93.5 – 95.9)	75.0
Good ECG Signal	79.9% (95% CI: 76.9 – 82.7)	75.0	91.4% (95% CI: 88.9 – 93.3)	75.0

Examples shown below are user interface design for taking a recording and displaying analysis results in using Eko stethoscope mobile application.

Figure 1: Example User Interface Design



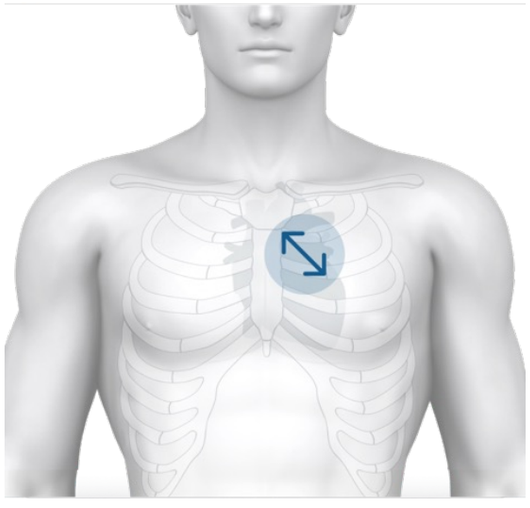
ANALYSIS USAGE

Note that the Eko Low Ejection Fraction Tool has been tested on ECGs captured from modified Lead II. A high-quality ECG signal must be present.

Standard procedures for ECG data capture should be followed including background noise reduction and optimal patient positioning when capturing data for the Eko Low Ejection Fraction Tool. The quality of the ECG is dependent on proper preparation practices including body hair, skin dryness, and clean contact area.

The diagram below is an example of positioning for optimal placement and orientation of electrodes to capture the necessary ECG vector (modified Lead II). The electrodes are placed over the left pectoral muscle, centered below the clavicle and angled towards the right shoulder.

Figure 2. Example of optimal placement and orientation of electrodes to capture ECG vector (modified Lead II).



3.0
Performance Data - Clinical Testing

Eko Low Ejection Fraction Tool (ELEFT) performance has been validated on a proprietary database. The database contains paired ECG and heart sound recordings and echocardiograms from 3,456 unique subjects. The paired ECG and heart sound recordings were captured with the Eko DUO digital stethoscope placed in a modified Lead II orientation. No complications or adverse events were experienced during the use of the ELEFT device. The prevalence of heart failure risk factors in the ELEFT test dataset is shown below in Table 2. The risk factors of heart failure, according to 2022 American Heart Association(AHA) guidelines1, include but are not limited to those with: coronary artery disease; diabetes mellitus; cardiomyopathy; hypertension; and obesity.

Table 2: Prevalence of heart failure risk factors in ELEFT test dataset

Heart failure risk factor	n(%)*
Hypertension	2459(71.2)
Coronary artery disease	1426(41.3)
Diabetes mellitus	960(27.8)
Cardiomyopathy	625(18.1)
Obesity (BMI≥30)	1563(45.2)
Permanent atrial fibrillation	75(2.2)
Chronic obstructive pulmonary disease	295(8.5)
Renal failure	258(7.5)
Obstructive sleep apnea	429(12.4)
Left bundle branch block	156(4.5)
Receiving cardiotoxic drugs	26(0.8)
Aortic stenosis	160(4.6)
Myocardial infarction	524(15.2)

Ground truth for classification was obtained from gold standard echocardiogram. All subjects underwent echocardiography within a maximum of 7 days of the corresponding ECG and heart sound recordings. The subject's true ejection fraction was measured by a cardiac technician using the echocardiogram machine's integrated cardiac quantification software at the time of the echocardiogram and then overread by a board-certified cardiologist. Ejection fraction status was then assigned by categorizing the subject's measured ejection fraction into Low EF (≤40%) or Normal EF (> 40%).

Based on these two categories, 9.9% of recordings came from subjects with confirmed Low EF and 90.1% of recordings came from subjects with confirmed Normal EF.

The following table (Table 3) demonstrates the results of the primary performance analysis (Low EF Detection):

Table 3: Summary Clinical Performance of ELEFT

	Sensitivity (%)	Specificity (%)
Low EF Detection	74.7 (95% CI: 69.4-79.6)	77.5 (95% CI: 75.9-79.0)

3.1
Summary-Level Descriptions of Patient Demographics for Training Dataset

Eight sites within the US (n = 7) and India (n = 1) contributed training data from 1,515 and 337 patients, respectively. The median age in the training dataset was 66 (IQR 51-75). 51.3% (951) of patients were male and 45.7% (847) were female, while gender was unknown for the remaining 2.9% (54). The majority of patients were White (1,089 [58.8%]), followed by Black or African American (65 [3.5%]), Asian (423 [22.9%]), American Indian or Alaska Native (2 [0.1%]), Other (24 [1.3%]), Native Hawaiian or Other Pacific Islander (3 [0.2%]), and Unknown (246 [13.3%]).

A total of 201 cases of EF ≤40% were identified from the 1,852 patients (prevalence 10.9%).

3.2 Summary-Level Descriptions of Patient Demographics for Test Dataset

Five sites within the US (n = 4) and India (n = 1) contributed data from 2,960 and 496 patients, respectively. For the prevalence of heart failure risk factors, see Table 2. The median age in the sample was 64 (IQR 52-73), and 44.3% (1,530) of patients were female. The majority of patients were White (2,011[58.2%]), followed by Black or African American (748 [21.6%]), Asian (517 [15.0%]), American Indian or Alaska Native (28 [0.8%]), Other (147 [4.3]), and Native Hawaiian or Other Pacific Islander (5, 0.1%) and therefore representative of the intended use population.

In this sample, 307 records were excluded as a result of poor ECG quality, and a total of 341 cases of EF ≤40% were identified from 3,456 samples (prevalence 9.9%). ELEFT achieved a sensitivity of 74.7% (95%CI: 69.4-79.6), a specificity of 77.5% (95%CI: 75.9-79.0), a positive predictive value (PPV) of 25.7% (95%CI: 22.8-28.7), and a negative predictive value (NPV) of 96.7% (95%CI: 95.9 to 97.4).

3.2.1 Associated Subgroup Analyses

Subgroup assessments of diagnostic performance were conducted to determine if there was heterogeneity in device performance across patient demographics, including conduction disorders. The results are summarized in Table 4 below.

Table 4: Clinical Performance in Pre-Specified Subgroup Analyses

Subgroup	Results of Test Heterogeneity
Age	Age was stratified into four groups: 18-30, 31-50, 51-70, >70 years. While no significant differences in sensitivity were observed among the age groups, the specificity of tests for patients aged >70 years (70.7% [95%CI: 67.8-73.5]) showed a slightly lower value compared to those performed on patients aged 31-50 (80.9% [95%CI: 77.3-84.3]) and 51-70 (81.1% [95%CI: 78.8-83.2]). Elderly patients are more likely to have several cardiac comorbidities, potentially resulting in higher rates of false positives.
Biological sex	Specificity varied slightly across biological sex (male: 73.6% [95% CI: 71.3-75.8] vs female: 81.8% [95% CI: 79.7-83.9]. However, this may not reflect a true difference, as the values may be confounded by the higher prevalence of cardiac comorbidities in the male subgroup (15.6% vs. 11.5%).
Body-Mass-Index (BMI)	BMI was stratified into six categories: <18.5, 18.5-24, 25-29, 30-34, 35-39, >=40 kg/m2. No significant differences were observed.
Race/ethnicity	No significant differences were observed.
Conduction disorders	In patients with pacemakers or cardiac comorbidities (e.g., [permanent] atrial fibrillation, left bundle branch block, wide QRS complex [>120ms]), there was an overall trend toward increased sensitivity, however this was not significant. Specificity, conversely, was lower for patients with the above comorbidities. These comorbidities are known to cause variations in ECG morphology, resulting in higher rates of false positives in these subgroups.

4.0
Technical Specification

Eko Low Ejection Fraction Tool is compatible with heart sound and ECG data recorded by Eko DUO Digital Stethoscope and the CORE 500 Digital Stethoscope, in which the recorded data satisfies the following technical specifications:

Table 5: Technical Specification of ELEFT Data Input Characteristics.

Feature	Value
PCG Input Characteristics	
Recording length	15s
PCG sensor technology	Digital MEMS microphone
Audio sampling rate	4000 Hz
Audio resolution	16 bit
Audio lossy signal compression	None
Audio Nyquist frequency	2000 Hz
Audio Frequency range where amplitude response is greater than -3dB (relative to max amplitude response)	70 - 300 Hz (minimum requirement)
Diaphragm placement	Upper left sternal border
ECG Input Characteristics	
ECG sampling rate	500 Hz
ECG resolution	16 bit
ECG lossy signal compression	None
ECG Nyquist frequency	250 Hz
ECG Frequency range where amplitude response is between -3dB to +3dB (relative to response at 5Hz)	0.67 - 40 Hz (minimum requirement)
ECG electrode material	Stainless steel
ECG electrode spacing	45 - 55 mm
Electrode placement	AN orientation: Upper left sternal border - modified Lead II orientation

5.0
System Requirements

Below is a summary of the required system requirements and specifications for mobile devices which display results provided by the ELEFT algorithm.

Table 6: System Requirements

Platform	Platform Compatibility
Android	Android 11 (API level 30) and above Android SDK version 30 BLE 4.2 and above
iOS	iOS version 15 and above Xcode version 14.3.1 and above BLE 4.2 and above

Eko maintains a public-facing website that details all necessary system requirements for enterprise customers. These support pages are reviewed and updated as part of the quarterly cybersecurity review. These pages outline the following:

- Eko Security Overview
- Port and Protocol whitelist requirements
- Customer Network Administration requirements
- Single Sign On configuration

Additionally, Eko Health has a dedicated customer support web page that provides third-party integrators with up-to-date details related to requirements for system compatibility, port and protocol whitelist, and Eko security overview. Eko has a dedicated Web page for customer support: support.ekohealth.com

The third-party integrator user manual is available on ekohealth.com/ifu and upon request.

To report security and privacy issues or concerns, Customers can contact: security@ekohealth.com or privacy@ekohealth.com.

References

1. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

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