Original Article

The HEART Pathway Randomized Trial

Identifying Emergency Department Patients With Acute Chest Pain for Early Discharge

2022.03.12

別役　翼

Circ Cardiovasc Qual Outcomes. 2015 Mar;8(2):195-203.

HEART pathway：急性冠症候群が疑われる胸痛患者のうち早期に帰宅可能な患者を特定するプロトコル

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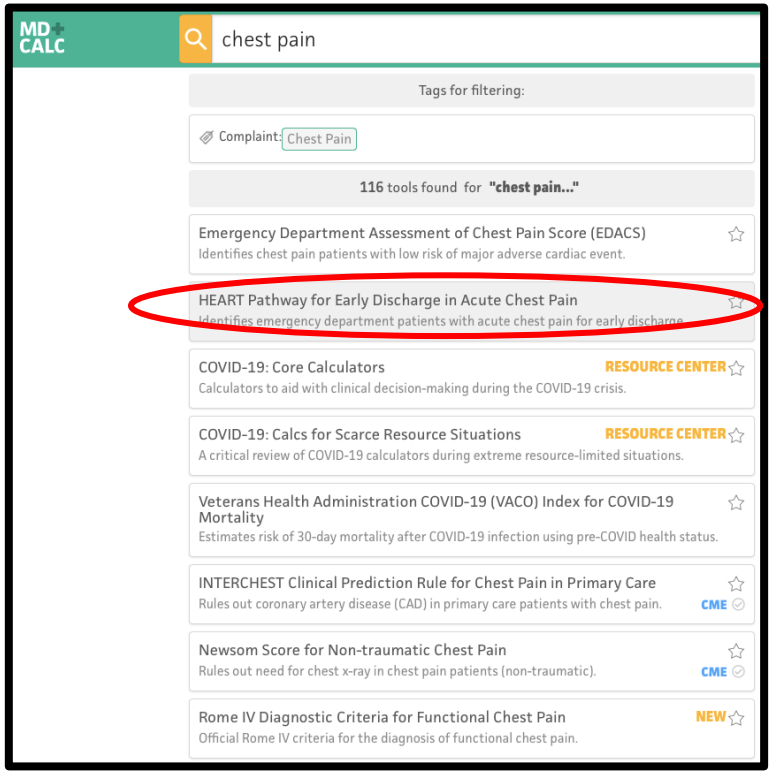
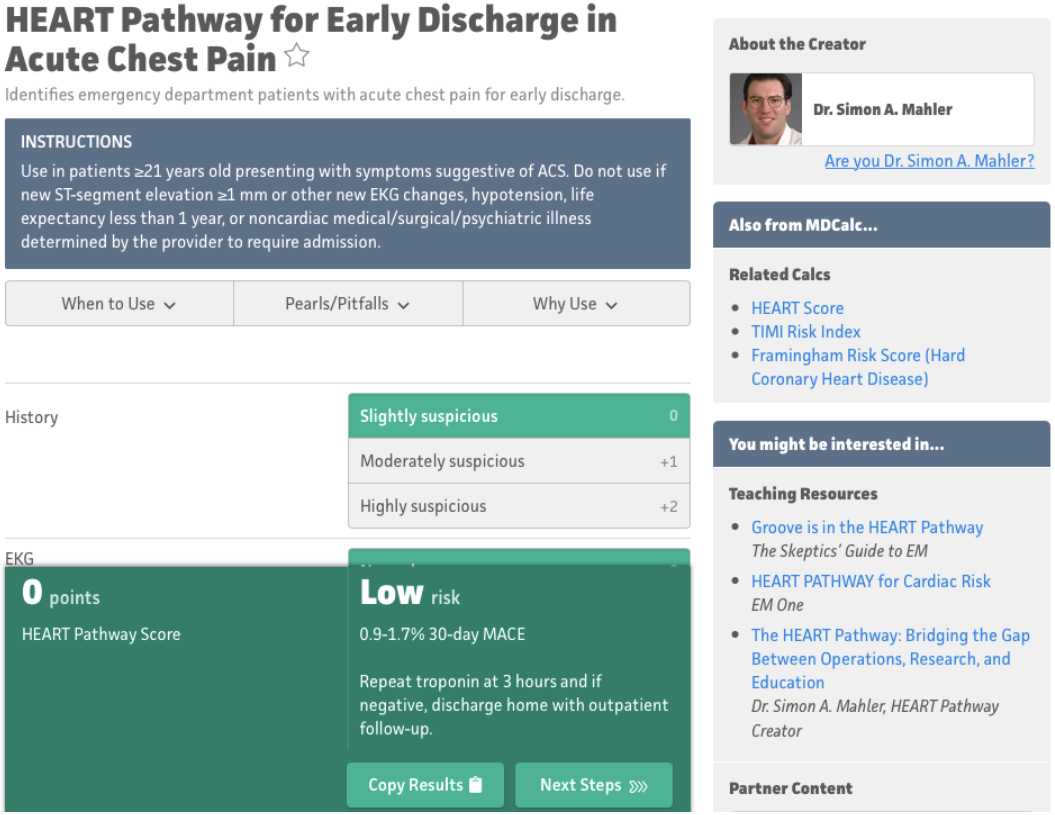
https://www.mdcalc.com/heart-pathway-early-discharge-acute-chest-pain





HEART pathwayは本当に早期帰宅可能なACS低リスク患者を同定し、胸痛患者の安全な管理に寄与するか？

1.論文のPICOは何か？

WHAT IS KNOWN

- Current care patterns for low-risk patients with acute chest pain are inefficient and expensive; they result in high hospitalization and stress testing rates while identifying few patients with acute coronary syndrome.
- Prospective observational and retrospective studies suggest that the HEART Pathway can safely identify low-risk patients with acute chest pain for early discharge from the emergency department without stress testing or coronary angiography.

WHAT THE STUDY ADDS

- This is the first clinical trial to examine the real-time use of the HEART Pathway to guide chest pain risk stratification and disposition decisions.
- Use of the HEART Pathway at the Wake Forest Baptist Medical Center compared with usual care among patients with acute chest pain produced significant reductions in objective cardiac testing during 30 days, hospitalizations, and index hospital length of stay.
- None of the patients identified for early discharge from the emergency department with the HEART Pathway had an adverse cardiac event at 30 days.

event (MACE) rate of >99% at 30 days.[13,14] However, the real-time use of the HEART Pathway has yet to be compared with usual care. Therefore, we have designed a randomized controlled trial to evaluate the efficacy of the HEART Pathway to guide providers' testing and disposition decisions for patients with acute chest pain. We seek to determine whether the HEART Pathway can meaningfully reduce objective cardiac testing, increase early discharges, and reduce index hospital length of stay (LOS) compared with usual care while maintaining high sensitivity and NPV (>99%) for MACE.

Methods

Study Design

We conducted a randomized controlled single-center clinical trial funded by the American Heart Association from 9/2012-2/2014. All participants provided witnessed written informed consent and were randomized to the HEART Pathway or usual care strategies. In the HEART Pathway arm, ED attending physicians used the HEART Pathway to guide testing and disposition decisions. In the usual care arm, providers were encouraged to follow American College of Cardiology guidelines.[12,13] This trial was approved by the Internal Review Board of the sponsoring organization and was registered with clinicaltrials.gov (clinical trial number, NCT01665521) before enrollment.

Setting

Participants were recruited from the ED (of institution name withheld for review). The study institution is a tertiary care academic medical center located in the Piedmont Triad area of North Carolina, serving urban, suburban, and rural populations. The ED is staffed by board-certified or board-eligible emergency physicians 24 hours per day, 7 days a week who directly provide care and oversee care provided by residents, physician assistants, and nurse practitioners. ED patient volume in 2013 consisted of ≈104 000 patient encounters. Cardiac testing modalities routinely available to study participants included exercise stress echocardiogram, dobutamine stress echocardiogram, coronary computed tomographic angiography, stress nuclear imaging, stress cardiac magnetic resonance imaging, or invasive coronary angiography. Serum troponin measurements were performed using the ADVIA Centaur platform TnI-Ultra™ assay (Siemens, Munich, Germany), which has a 99th percentile of the upper reference limit and 10% coefficient of variation at 0.04 mg/L.

Participants

Patients ≥21 years old presenting with symptoms suggestive of ACS were screened during enrollment hours (6 days excluding Saturday, 80 hours per week). Eligibility criteria included the provider ordering an ECG and troponin for the evaluation of ACS. Patients were determined ineligible for the following reasons: new ST-segment elevation ≥1 mm, hypotension, life expectancy <1 year, a noncardiac medical, surgical, or psychiatric illness determined by the provider to require admission, previous enrollment, non-English speaking, and incapacity or unwillingness to consent.

Randomization

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Randomization Arms

HEART Pathway

Participants were randomized to the HEART Pathway or usual care arms. Within the HEART Pathway arm, participants were risk stratified by attending ED providers using a validated clinical decision aid, the HEART score,[6–10] and serial troponin measures at 0 and 3 hours after ED presentation. The HEART score consists of 5 components: history, ECG, age, risk factors, and troponin (Appendix 1). To calculate a HEART score, first each component is assessed (on a scale of 0–2), and then component scores are summed to produce the final score. A HEART score of 0 to 3 is consistent with a low-risk assessment, whereas a score of ≥4 is consistent with a high-risk assessment. To facilitate HEART score completion, study staff provided the physician with the participant's ECG and a worksheet (Appendix 1) to complete at the bedside for each patient. On the basis of the HEART score and serial troponin results, the attending physicians received care recommendations according to the HEART pathway (Figure 1). For patients with low-risk HEART scores (HEART score of 0–3) and

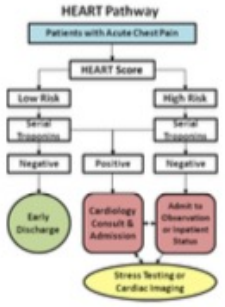

Figure 1. HEART Pathway algorithm.

Patient

- 心電図およびトロポニン測定が可能な施設において21歳以上でACSが示唆された患者

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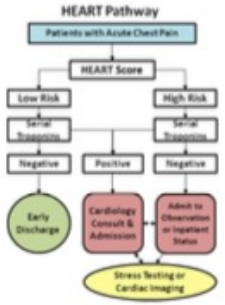

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Patient

重要な除外項目

- 1mm以上の新規ST上昇
- 低血圧
- 1年以内の予後
- 非心疾患の疾患で入院が必要と判断された患者
- 過去のエントリー
- 英語ができない患者
- 同意が取れない患者

Excluded (n=4721)
- Not meeting inclusion criteria (n=4284)
- Declined to participate (n=137)
- Attending survey not completed (n=74)
- No study investigator available (n=171)
- Other (n=55)

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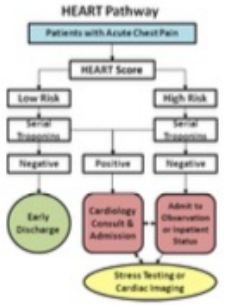

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Intervention

- HEART scoreと受診後0時間・3時間の連続トロポニン測定
- HEART score 0-3なら低リスク
- HEART score>=4なら高リスク
- 低リスクなら救急外来から退院してプライマリケアでのフォローアップを推奨
- 高リスクもしくはトロポニン高値なら心臓検査を推奨

1.論文のPICOは何か？

Appendix 1. HEART Pathway Assessment Form

HEART Score:

Patient ID _____
☐ Initial Assessment
☐ Second Assessment

History:

High-Risk Features:
- Middle- or left-sided
- Heavy chest pain
- Diaphoresis
- Radiation
- N/V
- Exertional
- Relief of symptoms by sublingual nitrates

Low-Risk Features:
- Well localized
- Sharp pain
- Non-exertional
- No diaphoresis
- No N/V

☐ Highly Suspicious	**2 points**	**Mostly high-risk features**
☐ Moderately Suspicious	**1 point**	**Mixture of high-risk and low-risk features**
☐ Slightly Suspicious	**0 points**	**Mostly low-risk features**

ECG:

☐ New ischemic changes	**2 points**	• Ischemic ST-segment depression • New ischemic T-wave inversions
☐ Non-specific changes	**1 point**	• Repolarization abnormalities • Non-specific T wave changes • Non-specific ST-segment depression or elevation • Bundle branch blocks • Pacemaker rhythms • LVH • Early repolarization • Digoxin effect
☐ Normal	**0 points**	• **Completely normal**

Age:

☐ ≥ 65	**2 points**
☐ 45-64	**1 point**
☐ <45	**0 points**

Risk Factors:
- ☐ Obesity (BMI ≥30)
- ☐ Current or recent (≤90 days) smoker
- ☐ Currently treated diabetes mellitus
- ☐ Family history of CAD (1st degree relative <55 y.o.)
- ☐ Diagnosed and/or treated hypertension
- ☐ Hypercholesterolemia

☐ 3 or more risk factors listed above **OR** any of the following: ☐ Known CAD=2 points ☐ Prior stroke=2 points ☐ Peripheral arterial disease = 2 points	**2 points**
☐ 1-2 risk factors	**1 point**
☐ No risk factors	**0 points**

Troponin (initial)

☐ >0.120 ng/ml	**2 points**
☐ 0.041-0.120 ng/ml	**1 point**
☐ 0-0.040 ng/ml	**0 points**

HEART Score (total points) _____ Add points from each category above

Serial 3 Hour Troponin Measurement:
- ☐ Normal, 0-0.040 ng/ml
- ☐ Positive, >0.040 ng/ml

HEART Pathway:
- ☐ High Risk = HEART score 4 or more, or any positive troponin.
- ☐ Low Risk = HEART score 0-3 and negative troponins at 0 and 3 hours

Attending Signature: _____ Date: _____
Attending Name: _____

Intervention：HEART pathway form

[HEART pathwayの構成要素]
- 病歴
- 心電図
- 年齢
- 危険因子
- トロポニン

1.論文のPICOは何か？

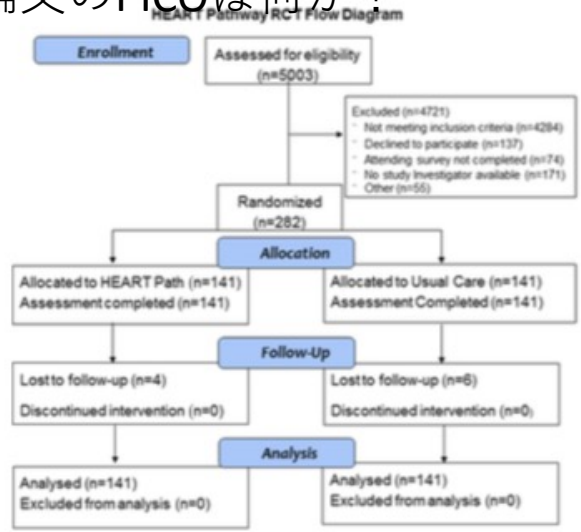

Figure 2. Enrollment flow diagram.

negative troponin results, the HEART pathway recommends discharge from the ED without further testing. These patients were encouraged to follow up with their primary care provider. In patients with a high-risk HEART score (HEART score of ≥4) or troponin above the 99th percentile threshold, the HEART Pathway recommends further evaluation (objective cardiac testing) in the hospital or observation unit (OU). For patients with an elevated troponin measurement or inducible ischemia on objective cardiac testing, the HEART pathway recommended cardiology consultation and admission to the hospital.

Usual Care

Care delivery in the usual care arm was at the discretion of the ca providers and not determined by the trial protocol. However, provider were encouraged to follow American College of Cardiology/America Heart Association guidelines,[11,20,21] which recommend serial cardia biomarkers and objective cardiac testing before discharge from the O or inpatient ward for patients with symptoms suggestive of ACS.[16,23]

HEART Pathway Adherence

Care delivered in both randomization arms was ultimately determined by provider discretion and not mandated by the trial protocol. The HEART Pathway was used by providers, in a manner consistent with its intent, as a decision aid rather than a substitute for clinical judgment. Therefore, some nonadherence to the care delivery described in Figure 1 was anticipated. To quantify and examine the effect of nonadherence on our outcomes, the number of patients in the HEART Pathway arm receiving adherent or nonadherent care was determined.

HEART Score Interobserver Agreement

Patients randomized to the HEART Pathway received a second HEART score assessment by an attending physician study investigator blinded to the initial assessment by the patient's attending physician. Based on our Institutional Review Board recommendations, if a disagreement occurred in which the attending provider determined the patient to be low-risk, but the study investigator found the patient to be high-risk, the attending provider was made aware of this discrepancy.

Data Collection and Processing

Our trial was conducted in accordance with standards of good clinical practice, standardized reporting guidelines,[24] and key data elements and definitions.[25] A detailed source of data map was created before study initiation. Electronic medical records were used as the source for data elements reliably contained in the medical record. Research Electronic Data Capture data collection templates were used to prospectively collect and store data from patients and care providers for data elements not reliably present in the electronic medical records.

Follow-up was conducted during the index visit using structured record review. At 30 days, a structured record review was followed by a telephone interview using a validated scripted follow-up dialogue[26] to further clarify events since discharge, identify events occurring at other care facilities, and to determine healthcare utilization since discharge. Outcome events reported at other healthcare facilities were confirmed using a structured review of those medical records. Incomplete follow-up at 30 days was handled using the following algorithm: participants with ongoing visits in the electronic medical records were considered to have complete information and were classified on the basis of data available in the medical record; participants with no ongoing visits were considered lost to follow up at the point of last contact. The Social Security Death Master File was used to search for participants unable to be contacted. In the event of discrepancy between a participant's self-reported event and the medical record, the medical record was considered correct.

Outcomes

Healthcare Utilization

Our primary outcome was the rate of objective cardiac testing within 30 days of presentation, defined as the proportion of patients receiving any stress testing modality, coronary computed tomographic angiography, or invasive coronary angiography at the index visit or within 30 days. Secondary outcomes included early discharge rate, index LOS, and cardiac-related recurrent ED visits and nonindex hospitalization at 30 days. Early discharge was defined as discharge from the ED without objective cardiac testing. Hospitalization was defined as bedding a patient to an OU or inpatient ward in observation or inpatient status. LOS was recorded from the electronic medical records and represented the time from patient placement into an ED bed to hospital discharge. A cardiac-related recurrent ED visit was defined as any patient revisiting the ED with chest pain or other symptoms suggestive of ACS within the 30-day follow-up period. Thirty-day nonindex hospitalization was defined as an inpatient or OU evaluation for ACS within 30 days.

Comparison

- プロトコルには定めておらず、各々の裁量に従って医療提供された
- ACC/AHAガイドラインにそっての診療を推奨された

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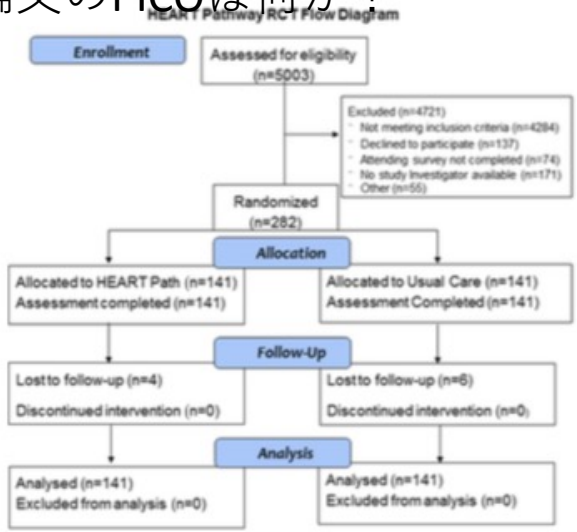

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Outcome

Primary outcome

来院後30日以内に客観的心臓検査を受けた割合 ：ストレス検査，冠動脈コンピュータ断層撮影，侵襲的冠動脈造影を受けた患者の割合と定義

Secondary outcome

1. 早期退院率(早期退院：客観的な心臓検査を行わずに救急外来から退院すること)
2. 入院期間(入院：観察ユニットまたは入院病棟に観察または入院状態で患者を寝かせること、LOS：患者がEDのベッドに寝かされてから退院するまでの期間)
3. 30日経過時点の心臓関連のED再診および入院 (心臓関連のED再診：30日のフォローアップ期間内に胸痛やACSを示唆する他の症状でEDを再訪した患者 、 30日以内の入院：30日以内にACSのために入院またはOU評価を受けたもの)

2.ランダム割付されているか？

WHAT IS KNOWN

- Current care patterns for low-risk patients with acute chest pain are inefficient and expensive; they result in high hospitalization and stress testing rates while identifying few patients with acute coronary syndrome.
- Prospective observational and retrospective studies suggest that the HEART Pathway can safely identify low-risk patients with acute chest pain for early discharge from the emergency department without stress testing or coronary angiography.

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- This is the first clinical trial to examine the real-time use of the HEART Pathway to guide chest pain risk stratification and disposition decisions.
- Use of the HEART Pathway at the Wake Forest Baptist Medical Center compared with usual care among patients with acute chest pain produced significant reductions in objective cardiac testing during 30 days, hospitalizations, and index hospital length of stay.
- None of the patients identified for early discharge from the emergency department with the HEART Pathway had an adverse cardiac event at 30 days.

event (MACE) rate of >99% at 30 days.[13,14] However, the real-time use of the HEART Pathway has yet to be compared with usual care. Therefore, we have designed a randomized controlled trial to evaluate the efficacy of the HEART Pathway to guide providers' testing and disposition decisions for patients with acute chest pain. We seek to determine whether the HEART Pathway can meaningfully reduce objective cardiac testing, increase early discharges, and reduce index hospital length of stay (LOS) compared with usual care while maintaining high sensitivity and NPV (>99%) for MACE.

Methods

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Setting

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Randomization Arms

HEART Pathway

Participants were randomized to the HEART Pathway or usual care arms. Within the HEART Pathway arm, participants were risk stratified by attending ED providers using a validated clinical decision aid, the HEART score,[9–15] and serial troponin measures at 0 and 3 hours after ED presentation. The HEART score consists of 5 components: history, ECG, age, risk factors, and troponin (Appendix 1). To calculate a HEART score, first each component is assessed (on a scale of 0–2), and then component scores are summed to produce the final score. A HEART score of 0 to 3 is consistent with a low-risk assessment, whereas a score of ≥4 is consistent with a high-risk assessment. To facilitate HEART score completion, study staff provided the physician with the participant's ECG and a worksheet (Appendix 1) to complete at the bedside for each patient. On the basis of the HEART score and serial troponin results, the attending physicians received care recommendations according to the HEART pathway (Figure 1). For patients with low-risk HEART scores (HEART score of 0–3) and

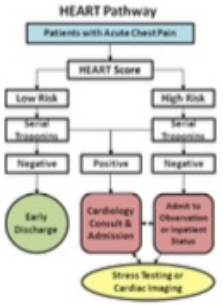

Figure 1. HEART Pathway algorithm.

- 既知の冠動脈疾患（血行再建術の既往を含む）の有無によって層別化→ランダム置換ブロック法にて等確率で割付
- 治験責任医師およびスタッフは、無作為化順序について盲検化 (無作為化順序はnQuery Advisor 6.0（Statistical Solutions, Saugus, MA）を用いて作成)

Table 1. HEART Pathway Randomized Controlled Trial Patient Characteristics

3.Base Lineは同等か？

	HEART Pathway		Usual Care	
Patient Characteristics	Number, n=141	Percent	Number, n=141	Percent
Age, y, mean±SD	53.4±12.0	…	53.1±12.2	…
Sex				
Female	81	57.4	81	57.4
Race				
White	90	63.8	93	66.0
Black	48	34.0	46	32.6
Asian	1	0.7	0	0
Native American	1	0.7	1	0.7
Others	1	0.7	1	0.7
Ethnicity				
Hispanic	1	0.7	4	2.8
Non-Hispanic	140	99.3	137	97.2
Risk factors				
Current smoking	42	29.8	34	24.1
Recent cocaine (last 90 days)	3	2.1	3	2.1
Hypertension	75	53.2	82	58.2
Hyperlipidemia	61	43.3	60	42.6
Diabetes mellitus	31	22.0	27	19.2
Family history of coronary disease	44	31.4	58	41.4
BMI, >30 kg/m^2	71	50.4	81	57.5
TIMI risk score, >1	60	42.6	63	44.7
Previous coronary disease	28	19.9	29	20.6
Previous MI	21	14.9	24	17
Previous PCI	14	9.9	19	13.5
Previous CABG	7	5.0	3	2.1
Previous cerebral vascular disease	3	2.1	9	6.4
Previous peripheral vascular disease	4	2.8	4	2.8
Insurance status				
Insured	105	74.5	106	76.3
Private	71	50.4	68	48.9
Medicare	21	14.9	21	15.1
Medicaid	13	9.2	17	12.2
Uninsured	36	25.5	33	23.7

BMI indicates body mass index; CABG, coronary artery bypass graft; MI, myocardial infarction; PCI, percutaneous coronary intervention; and TIMI, thrombolysis in myocardial infarction.

4. すべての患者の転帰がoutcomeに反映されているか？

4-1 ITT解析か？

- 全てのアウトカムはITT解析

Table 1. HEART Pathway Randomized Controlled Clinical Trial Study Population

Patient Characteristics	HEART Pathway Number, n=141	HEART Pathway Percent	Usual Care Number, n=141	Usual Care Percent
Age, y, mean±SD	53.4±12.0	…	53.1±12.2	…
Sex				
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Race				
White	90	63.8	93	66.0
Black	48	34.0	46	32.6
Asian	1	0.7	0	0
Native American	1	0.7	1	0.7
Others	1	0.7	1	0.7
Ethnicity				
Hispanic	1	0.7	4	2.8
Non-Hispanic	140	99.3	137	97.2
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BMI indicates body mass index; CABG, coronary artery bypass graft; MI, myocardial infarction; PCI, percutaneous coronary intervention; and TIMI, thrombolysis in myocardial infarction.

Safety Events

All participants were monitored for MACE, defined by a composite end point of all-cause mortality, myocardial infarction, or coronary revascularization within the 30-day follow-up period. Myocardial infarction was defined on the basis of Universal Definition of Myocardial Infarction.[21] Coronary revascularization was defined as angioplasty with or without stent placement or coronary artery bypass surgery. MACE occurring in patients discharged without objective cardiac testing was considered a missed MACE. All safety events were reviewed by the Institutional Data Safety Monitoring Board.

End Point Adjudication

A consensus of 2 reviewers (C.D.M. and B.C.H.), blinded to treatment arm assignment, adjudicated the elements required to measure the occurrence of MACE and to determine cardiac-relatedness of recurrent ED visits and nonindex hospitalizations. To make these assessments, reviewers were provided participant's index and discharge records, follow-up call information, records obtained from follow-up, and study definitions. Any disagreements were settled by consensus between the 2 reviewers or the involvement of a third reviewer.

Statistical Analysis

The proportion of patients receiving objective cardiac testing within 30 days, early discharge, and cardiac-related ED visits and nonindex hospitalizations were estimated for the HEART Pathway and usual care groups and a 95% confidence interval for the differences between the 2 groups was calculated using exact calculations. Unadjusted differences between groups in these outcomes at index and 30 days were assessed using the Fisher exact test. LOS was calculated for each participant and summarized using median and interquartile ranges for each treatment arm. LOS had a non-normal (right-skewed) distribution, so treatment arms were compared using Mann-Whitney *U* tests. With an expected rate of 83% in the usual care arm, this study was powered to detect a 15% reduction in objective cardiac testing within 30 days with 90% power at the 5% 2-sided level of significance with an expected loss to follow-up rate of 10%.

4. すべての患者の転帰がoutcomeに反映されているか？
4-2 脱落はどの程度か？

Table 1. Frequency of HEART Pathway Determinants

Risk Stratification Measure	Number	Percent
HEART score history		
Slightly suspicious (0 points)	52	36.9
Moderately suspicious (1 point)	54	38.3
Highly suspicious (2 points)	35	24.8
Age		
<45 (0 points)	38	27
45–65 (1 point)	80	56.7
>65 (2 points)	23	16.3
ECG		
Normal (0 points)	79	56
Nonspecific changes (1 point)	60	42.6
Changes consistent with ACS (2 points)	2	1.4
Number of risk factors		
0 (0 points)	16	11.4
1–2 (1 point)	58	41.1
≥3 (2 points)	67	47.5
Troponin (initial)		
Negative (0 points)	133	94.3
1–3× normal limit (1 point)	4	2.8
>3× normal limit (2 points)	4	2.8
Total HEART score		
0	3	2.1
1	9	6.4
2	28	19.9
3	27	19.1
4	31	22
5	21	14.9
≥6	22	15.6
Serial troponin at 3 h		
Negative	131	92.9
Positive	9	6.4
Missing	1	0.7
HEART Pathway		
Low risk (HEART score <3 and negative troponins at 0 and 3 h)	66	46.8
High risk (HEART score >3 or positive troponin at 0 or 3 h)	75	53.2

ACS indicates acute coronary syndrome.

Sensitivity, specificity, positive predictive value and NPV, and their exact 95% confidence intervals for MACE during the 30-day follow-up period were calculated for each treatment arm. In addition, to determine the incremental value of the HEART Pathway to serial troponin testing, the sensitivity, specificity, positive predictive value, and NPV of serial troponin results at 0 and 3 hours used alone (without the HEART score) were calculated. Missed MACE rates were estimated for the HEART Pathway and usual care groups, and an exact 95% confidence interval for the differences between the 2 groups was calculated. Unadjusted differences between groups in these outcomes at index and 30 days were assessed using the Fisher exact test. Patients with incomplete follow-up were considered to be free of 30-day MACE. Interobserver agreement for the HEART Pathway risk assessment was tested using a κ-statistic. Acceptable agreement was defined, a priori, as a κ of >0.60. To assess differences with the high- and low-risk HEART Pathway groups), the Kaplan–Meier method was used. All outcomes were analyzed using intention-to-treat. Statistical analysis was performed using SAS 9.3 (Cary, NC).

Results

From 9/2012-2/2014, 282 patients with symptoms suggestive of ACS were enrolled, with 141 randomized to each arm. No participants were removed from the study after randomization. Assessment for 30-day events was complete on 96% (272/282) of participants (Figure 2), with their characteristics summarized in Table 1. Of the 10 patients lost to follow up, none appeared in the Social Security Death Master File. Among the 141 patients randomized to the HEART Pathway, 46.8% (66/141) were risk stratified into a low-risk group and 53.2% (75/141) into a high-risk group. Interobserver agreement was acceptable (κ=0.63). The frequency of HEART Pathway determinants is summarized in Table 2.

Patients randomized to the HEART Pathway had a 30-day objective cardiac testing rate of 56.7% (80/141) compared with a rate of 68.8% (97/141) in the usual care group: an absolute reduction of 12.1% (P=0.048). Early discharge occurred in 39.7% (56/141) of patients in the HEART Pathway arm compared with 18.4% (26/141): an absolute increase of 21.3% (P<0.001). Patients in the HEART Pathway group had a median LOS of 9.9 hours compared with 21.9 hours in the usual care group (Figure 3): a median reduction in LOS of 12 hours (P=0.013).

Within the HEART Pathway arm, 2.8% (4/141) had cardiac-related repeat ED visits compared with 4.3% (6/141) in the usual care arm (P=0.75). Cardiac-related nonindex hospitalizations occurred in 3.6% (5/141) of patients in the HEART Pathway arm compared with 2.8% (4/141) in the usual care arm (P>0.999).

MACE occurred in 17 of 282 patients, with all events occurring during their index visit.

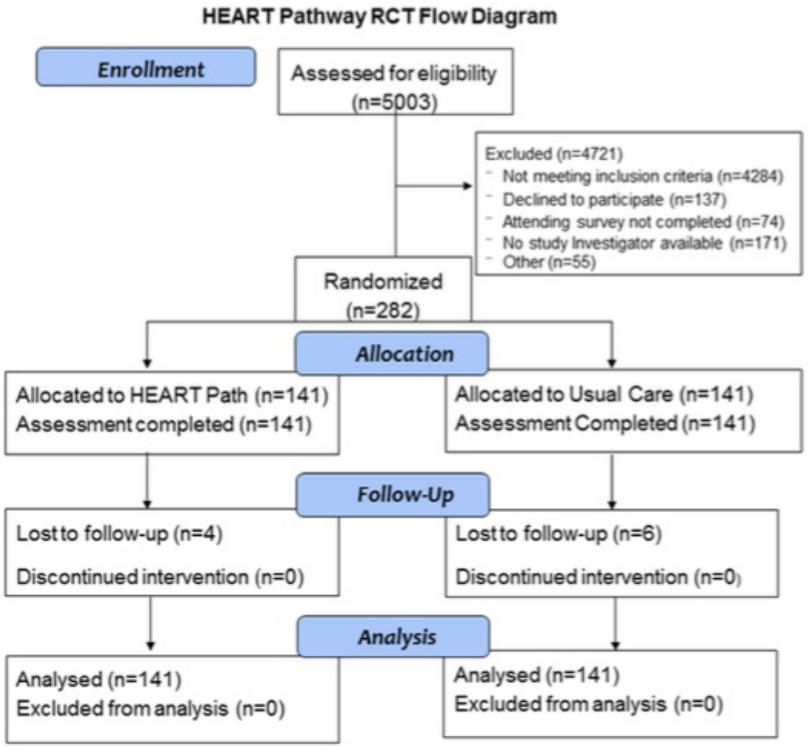
No patients identified for early discharge had missed MACE in either group during the 30-day follow-up period. No patients identified as low-risk by the HEART Pathway had an index or nonindex MACE. Index MACE occurred in 5.7% (8/141) patients in the HEART Pathway arm compared with 6.4% (9/141) in the usual care arm (P=1). Primary and secondary outcomes are summarized in Tables 3 and 4, respectively. The test characteristics of the HEART Pathway and serial troponins alone are summarized in Table 5. Nonadherence to the HEART Pathway occurred in 29% (19/66) of low-risk patients and 13% of (9/75) high-risk patients. None of the 19 low-risk patients had MACE at index or 30 days. Perfect adherence among high- and low-risk patients would have increased the early discharge rate to 46.8% (66/141).

Discussion

Results of this trial demonstrate that the HEART Pathway substantively reduces healthcare utilization (objective cardiac testing, hospitalization, and hospital LOS) among patients with symptoms related to ACS. Among patients with acute chest pain, the HEART Pathway produced a meaningful reduction in objective cardiac testing, doubled the ED rate of early discharge, and reduced the hospital LOS by half a day. Furthermore, these reductions in utilization outcomes were accomplished without

- Total 282人 (141人ずつ割り付け)
- それから除外された者なし

- 追跡不能：10人(死亡マスターファイルに記載なし)



5.マスキング(盲検化)されているか？

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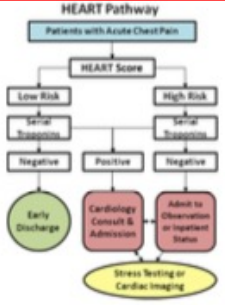

Figure 1. HEART Pathway algorithm.

- 治験責任者およびスタッフは無作為化順序を盲検化
- 盲検化された研究員による2回目のHEART score評価
- 盲検化された2人の審査員がMACE・ED再診・再診後の入院・心臓疾患との関連の判定

6.症例数は十分か？

Table 1. Primary and Adjudicated Confirmed MACE Patient Characteristics

Patient Characteristics	HEART Pathway Number, n=141	HEART Pathway Percent	Usual Care Number, n=141	Usual Care Percent
Age, y, mean±SD	53.4±12.0	…	53.1±12.2	…
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- 総患者数：282人
- 検出力(30日以内の客観的心臓検査の15％減少を検出)：90% (両側有意水準5%)

7.結果の評価

Primary end point

- HEART pathwayが使用された患者は通常ケアよりも検査が12.1%減少

Table 3. Objective Cardiac Testing at 30 Days

	HEART Pathway								
	Low-Risk Patients		High-Risk Patients		Total		Usual Care		
Outcomes	Number, n=66	Percent	Number, n=75	Percent	Number, n=141	Percent	Number, n=141	Percent	*P* Value*
Objective cardiac testing at 30 days	21	31.8	59	78.7	80	56.7	97	68.0	0.048
Positive	2	3.0	11	14.7	13	9.2	10	7.1	0.66
Negative	19	28.8	48	64.0	67	47.5	87	61.7	0.023
Type of objective cardiac testing									
CCTA	1	1.5	1	1.3	2	1.4	5	3.5	0.45
≥50% coronary stenosis	0	0	0	0	0	0	0	0	>0.999
<50% coronary stenosis	0	0	1	1.3	1	0.7	0	0	>0.999
No coronary stenosis	1	1.5	0	0	1	0.7	5	3.5	0.21
Indeterminate	0	0	0	0	0	0	0	0	…
Nuclear imaging	0	0	2	2.7	2	1.4	2	1.4	>0.999
Positive	0	0	2	2.7	2	1.4	1	0.7	>0.999
Negative	0	0	0	0	2	1.4	1	0.7	>0.999
Exercise stress echocardiogram	18	27.3	25	33.3	43	30.5	56	39.7	0.13
Positive	2	3.0	2	2.7	4	2.8	2	1.4	0.68
Negative	16	24.2	22	29.3	38	27.0	54	38.3	0.057
Nondiagnostic	0	0	1	1.3	1	0.7	0	0	>0.999
Dobutamine stress echocardiogram	2	3.0	13	17.3	15	10.6	23	16.3	0.22
Positive	0	0	0	0	0	0	1	0.7	>0.999
Negative	2	3.0	13	17.3	15	10.6	21	14.9	0.37
Nondiagnostic	0	0	0	0	0	0	1	0.7	>0.999
CMR	0	0	7	9.3	7	9.3	2	1.4	0.17
Positive	0	0	1	1.3	1	1.3	0	0	>0.999
Negative	0	0	6	8.0	6	8.0	2	1.4	0.28
Angiography	0	0	15	20.0	15	10.7	11	7.8	0.54
Coronary stenosis present, ≥70%	0	0	9	12.0	9	6.4	7	5.0	0.80
Coronary stenosis present, <70%	0	0	4	5.3	4	2.8	3	2.1	>0.999
No coronary stenosis	0	0	2	2.7	2	1.4	1	0.7	>0.999

CCTA indicates coronary computed tomographic angiography; and CMR, cardiac magnetic resonance.
*P value for comparison of the HEART Pathway total vs usual care.

Table 2. Frequency of HEART Pathway Determinants

Risk Stratification Measure	Number, n=141	Percent
HEART score history		
Slightly suspicious (0 points)	52	36.9
Moderately suspicious (1 point)	54	38.3
Highly suspicious (2 points)	35	24.8
Age		
<45 (0 points)	38	27
45–65 (1 point)	80	56.7
>65 (2 points)	23	16.3
ECG		
Normal (0 points)	79	56
Nonspecific changes (1 point)	60	42.6
Changes consistent with ACS (2 points)	2	1.4
Number of risk factors		
0 (0 points)	16	11.4
1–2 (1 point)	58	41.1
≥3 (2 points)	67	47.5
Troponin (initial)		
Negative (0 points)	133	94.3
1–3× normal limit (1 point)	4	2.8
>3× normal limit (2 points)	4	2.8
Total HEART score		
0	3	2.1
1	9	6.4
2	28	19.9
3	27	19.1
4	31	22
5	21	14.9
≥6	22	15.6
Serial troponin at 3 h		
Negative	131	92.9
Positive	9	6.4
Missing	1	0.7
HEART Pathway		
Low risk (HEART score <3 and negative troponins at 0 and 3 h)	66	46.8
High risk (HEART score >3 or positive troponin at 0 or 3 h)	75	53.2

ACS indicates acute coronary syndrome.

7.結果の評価　　Secondary end point

- 早期退院：39.7％（56/141人） vs 18.4％（26/141人） P<0.001
- LOS：9.9時間 vs 21.9時間　P=0.013
- ED再診：2.8％（4/141人） vs 4.3％（6/141人）　P=0.75
- Nonindex hospitalization：3.6％（5/141） vs 2.8％（4/141）　P>0.999

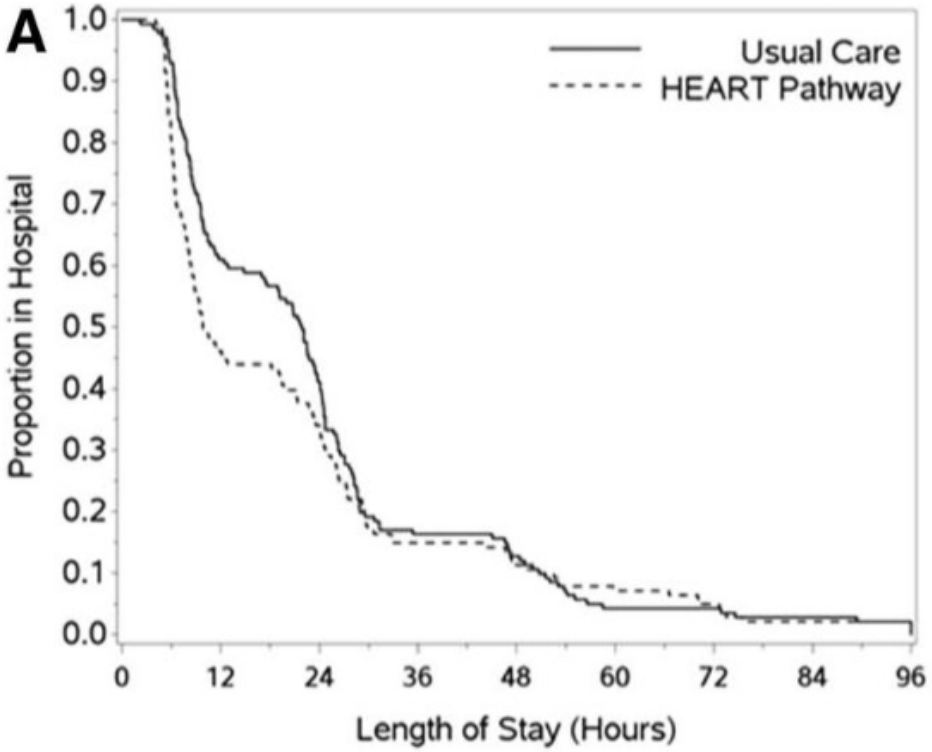
Table 4. Safety Events and Healthcare Utilization Outcomes

	HEART Pathway								
	Low-Risk Patients		High-Risk Patients		Total		Usual Care		
Outcomes	Number, n=66	Percent	Number n=75	Percent	Number, n=141	Percent.	Number, n=141	Percent	*P* Value*
Index length of stay, h; median (IQR)	6.4 (5.6–8.8)	…	25.9 (11.4–46.7)	…	9.9 (6.3–26.4)	…	21.9 (8.4–28.2)	…	0.013
Index visit disposition									
Hospitalization	19	28.8	66	88.0	85	60.3	110	78.1	0.002
Observation unit	18	27.3	25	33.3	43	30.5	62	44.0	0.31
Inpatient ward (admission)	1	1.5	41	54.7	42	29.8	48	34.0	0.52
Discharge	47	71.2	8	10.7	55	39.0	31	22.0	0.003
AMA	0	0	1	1.3	1	0.7	0	0	>0.999
Early discharge	47	71.2	9	12.0	56	39.7	26	18.4	0.0001
Recurrent hospital care at 30 days									
Repeat ED visit	2	3.0	8	10.7	10	7.1	18	12.8	0.16
Cardiac related	0	0	4	5.3	4	2.8	6	4.3	0.75
Nonindex hospitalization	1	1.5	8	10.7	9	6.4	9	6.4	>0.999
Cardiac related	0	0	5	6.7	5	3.6	4	2.8	>0.999
MACE at 30 days									
Cardiovascular death	0	0	0	0	0	0	0	0	…
MI	0	0	7	9.3	7	5.0	9	6.4	0.80
With revascularization	0	0	1	1.3	1	0.7	5	3.6	0.21
PCI	0	0	1	1.3	1	0.7	4	2.8	0.37
CABG	0	0	0	0	0	0	1	0.7	>0.999
Without revascularization	0	0	1	1.3	1	0.7	0	0	>0.999
PCI	0	0	1	1.3	1	0.7	0	0	>0.999
CABG	0	0	0	0	0	0	0	0	…

AMA indicates against medical advice; CABG, coronary artery bypass graft; ED, emergency department; IQR, interquartile range; MACE, major adverse cardiac event; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

7.結果の評価

Secondary end point



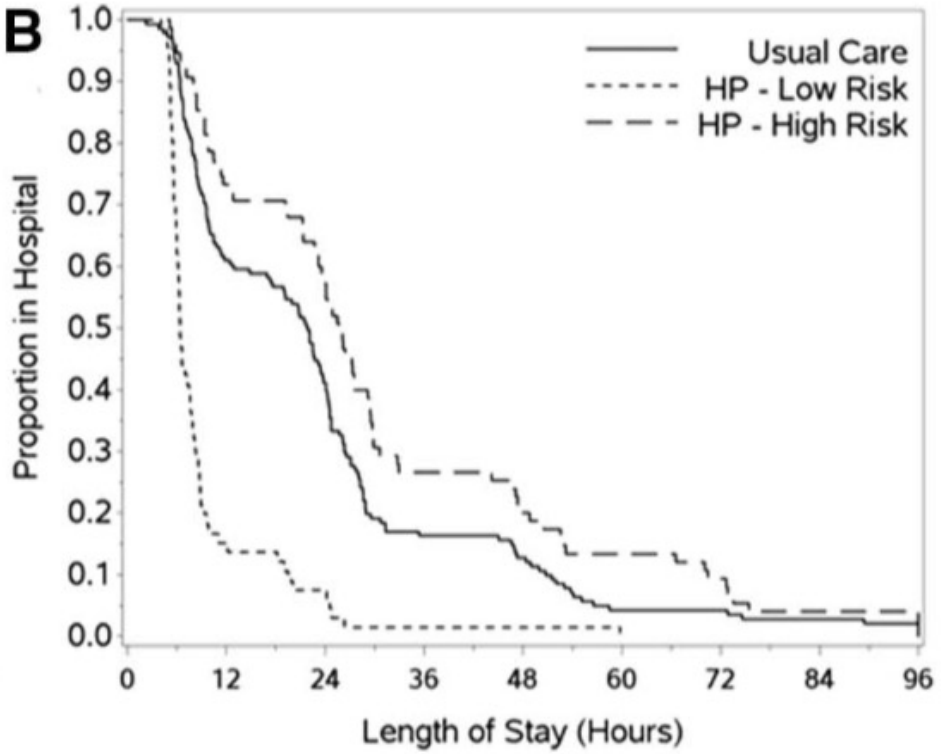


Table 5. Test Characteristics of the HEART Pathway and Serial Troponins

Risk Stratification Strategy	Early Discharge (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Serial troponins	92.2% (87.8–96.6)	87.5% (47.4–99.6)	97.0% (92.5–99.2)	63.6% (30.8–89.1)	99.2% (95.8–100)
HEART Pathway	39.7% (31.6–48.3)	100% (63.1–100)	49.6% (40.8–58.4)	10.7% (4.7–19.9)	100% (94.6–100)

NPV indicates negative predictive values; and PPV, negative predictive values.

長所

- 医療資源の効率的使用が可能
- 有害な血管イベントを見逃すことはない
- 臨床判断の代用ではなく、補助ツールとして機能
  (HEART pathway low riskでも検査されている)

短所

- サンプルサイズが小さい (Exclusion (not meeting inclusion criteria)が多い)
- 単一施設
- MACEの差を検出するための検出力を有していない
- 10人のフォローアップ漏れ
- 主治医が低リスクと判断した患者を治験責任医師が高リスクと判断した場合、主治医にこの不一致を知らせていた
  →Double checkが必要となっている！
- Open-label：コンタミの可能性＋主治医による意図的な操作の可能性
- 2015年の研究であり、高感度TnTの臨床応用が開始されていない時代の研究