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Can emergency physician gestalt "rule in" or "rule out" acute coronary syndrome: validation in a multi-center prospective diagnostic cohort study

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Abstract

Background

Chest pain is a common problem presenting to the Emergency Department (ED). Many decision aids and accelerated diagnostic protocols have been developed to help clinicians differentiate those needing admission from those who can be safely discharged. Some early evidence has suggested that clinician judgement or gestalt alone could be sufficient.

Objectives

Our aim was to externally validate whether emergency physician's gestalt could "rule in" or "rule out" acute coronary syndromes (ACS).

Methods

We performed a multi-center prospective diagnostic accuracy study including consenting patients presenting to the ED in whom the physician suspected ACS. At the time of arrival, clinicians recorded their perceived probability of ACS using a five-point Likert scale. The primary outcome was a diagnosis of ACS, defined as acute myocardial infarction or major adverse cardiac events (MACE) within 30 days.

Results

1,391 patients were included; 240 (17.3%) had ACS. Overall, gestalt had fair diagnostic accuracy with a C-statistic of 0.75 (95% CI 0.72-0.79). If ACS was "ruled out" in the 60 (4.3%) patients where clinicians perceived that the diagnosis was "definitely not" ACS, a sensitivity of 98.0% and negative predictive value (NPV) of 95.0% could have been achieved. If ACS was only "ruled out" in patients who also had no ECG ischemia and a normal initial cardiac troponin (cTn) concentration, 100.0% sensitivity and NPV could be achieved. However, this strategy only applied to 4.1% of patients. If patients with "probably not" ACS who had normal ECG and cTn were also "ruled out" (n=418, 30.8%), sensitivity fell to 86.2% with 99.2% NPV. Using gestalt "definitely" ACS to "rule in" ACS gave a specificity of 98.5% and positive predictive value of 71.2%.

Conclusion

Clinician gestalt is not sufficiently accurate or safe to either "rule in" or "rule out" ACS as a decision-making strategy. This study will enable emergency physicians to understand the limitations of our clinical judgement.

Introduction

Chest pain is a common problem in the Emergency Department (ED) representing over 5-6% of all attendances[1,2] and over 25% of all acute medical admissions.[1] Most of these patients do not have an acute coronary syndrome (ACS) with prevalence at 8-10%.[1,3]

Prompt identification of patients presenting with chest pain who have ACS ("rule in"), and exclusion of ACS in those who do not ("rule out"), is a priority. Multiple accelerated diagnostic protocols have been developed to assist and guide clinicians' decision-making. Many are now available including: the HEART score,[2,8] the Global Registry of Acute Coronary Events (GRACE) score,[9] the Thrombolysis and Myocardial Infarction (TIMI) score,[10] the Troponin only Manchester Acute Coronary Syndrome decision aid (T-MACS)[11] and the Emergency Department Assessment of Chest Pain Score (EDACS).[12] Recent work has focused on the use of highly sensitive cardiac troponin (hs-cTn) assays to rule out AMI early in the patient journey; these have been incorporated into 1-hour and 3-hour AMI rule out strategies recommended by the European Society of Cardiology.[13] However, whilst the "typicality of chest pain" has been shown to be of limited discriminatory value in the assessment of suspected ACS,[14,15] early evidence suggests that clinician's global diagnostic assessment or gestalt may be sufficient in "ruling in" or "ruling out" the diagnosis.[16,17]

One prospective study found no statistical difference between gestalt and the HEART score in identifying "low risk" patients for ACS "rule out".[18] Another found that clinician gestalt of "probably not" or "definitely not" ACS combined with a normal ECG and arrival troponin could effectively rule out 23.1% of patients presenting with suspected cardiac chest pain. The sensitivity of this strategy was 99.0% (95% Confidence Interval (CI) 94.6% - 100.0%) and negative predicative value (NPV) 99.1% (95% CI 93.7 - 99.9%). Incorporation of a normal hs-cTnT concentration on arrival increased the number of patients identified as low risk to 41.7% with no missed AMIs and a 1.6% incidence of major adverse cardiac events (MACE) at 30 days. The sensitivity of this strategy for MACE was 97.0% (95% CI 91.5 - 99.4%), and NPV 98.4% (95% CI 95.3 - 99.5%).[17]

The primary aim of our study was to externally validate the diagnostic accuracy of clinician gestalt for "ruling in" or "ruling out" ACS in adults presenting to the ED with suspected cardiac chest pain.

Methods

Study design:

The Bedside Evaluation of Sensitive Troponin (BEST) study was a prospective multi-center diagnostic accuracy study at eighteen hospitals, including adults presenting to the Emergency Departments with suspected ACS (Supplementary Appendix). This is a pre-planned secondary analysis of the BEST study. Ethical approval was obtained from the National Research Ethics Service (reference 14/NW/1344). Patients were recruited over a two and a half year period from February 2015 – July 2017.

Study setting and population:

We included adult patients (> 18 years) presenting to the ED with suspected cardiac chest pain peaking within the past 12 hours (symptoms compatible with the American Heart Association case definition for ACS),[19] that the treating physician identified as requiring investigation for ACS. Exclusion criteria were: patients with unmistakable ST elevation myocardial infarction, those whose symptoms peaked over 12 hours ago, those presenting with other non-ACS medical complaints necessitating hospital admission and patients unable to provide written informed consent.

Study protocol:

Potential participants meeting the study inclusion criteria were given verbal and written information about the study by an investigator. Written consent was obtained from all participants. Each patient had an ECG performed. Blood was drawn for cardiac troponin testing on arrival. The treating physician and study nurse, on a standardized study case report form at the time of inclusion in accordance with international standards, captured study specific key clinical data. Data were collected on multiple variables including patient demographics, past medical history including risk factors for cardiovascular disease, 12-lead ECG findings and the clinician's assessment or unstructured gestalt about the probability of ACS. The latter had to be stated by the clinician responsible for providing clinical care to the patient, and was recorded on a five point Likert scale as follows: "definitely not" ACS, "probably not" ACS, "could be" ACS, "probably" ACS and "definitely" ACS. This data was recorded at the time of initial review following assessment; clinicians were unblinded to both the ECG and initial cardiac troponin results but were blinded to serial cardiac troponin results and the final outcome. The ECG was available to clinicians at the time of their review; the

availability of the initial cardiac troponin was dependent on local factors influencing the time of the clinicians assessment and the return of the laboratory result. All patients underwent reference standard serial troponin testing over at least 3 hours (when high-sensitivity cardiac troponin assays were in use) or at least 6 hours (for contemporary assays).

Follow-up was conducted for 30 days. Patients were followed by the research team throughout their admission and were contacted by telephone, email, letter or in person after 30 days. If the patient could not be reached, follow up information was collected from their general practitioner.

Outcome measures:

The primary outcome was a diagnosis of ACS, defined as prevalent AMI or incident MACE at 30 days. MACE included all cause death, coronary revascularization and incident AMI. All outcomes were adjudicated by two investigators blinded to each other's adjudication and to clinician gestalt. AMI was diagnosed in accordance with the Third Universal Definition of Myocardial Infarction. This required a rise and/ or fall of cardiac troponin with at least one level above the 99th percentile for a healthy reference population.[20]

Data Analysis:

As the sample size for this study was driven by the primary analysis, no formal *a priori* sample size calculation was performed for this secondary analysis. However, the primary analyses were powered such that a diagnostic test with 100% sensitivity and negative predictive value (NPV) would achieve 95% confidence intervals with lower bounds that did

not fall below 95% for sensitivity and 99% for NPV. Estimating a prevalence of 10% and 5% loss to follow-up, this would be achieved with a total sample of 1,575 patients. Descriptive statistics and receiver operator characteristic (ROC) curve analysis were performed using IBM SPSS (version 23.0, Armonk, NY: IBM Corp.). Sensitivity, specificity, positive predictive value (PPV) and NPV were calculated using MedCalc (version 18.11.3, Ostend, Belgium).

Results

In total, 1,613 cases were screened from the BEST study for inclusion in this secondary analysis. The flow of participants and reasons for exclusion are shown in Figure 1. Of these patients, 207 (14.9%) were given an adjudicated diagnosis of AMI and additional 33 developed MACE within 30 days (including 5 cardiac deaths and 28 coronary revascularizations), giving a total of 240 (17.3%) patients meeting criteria for the target condition of ACS. The population was predominantly male (n=893, 64.2%) with and average age of 58.7 years (range 19 – 93, standard deviation 15.4). The population cardiovascular risk factors are shown in Table 1. The clinician recorded the presence of acute ischaemic features on the ECG in 99 (7.1%) patients and the initial troponin was greater than the 99th percentile in 344 (24.7%) cases.

Clinician gestalt had an area under the ROC curve of 0.75 (95% CI 0.72 - 0.79) for ACS. The proportion of patients with ACS stratified by clinician's gestalt is shown in Table 2. Despite being investigated for ACS, in 60 (4.3%) of cases, the clinician felt that ACS was actually "definitely not" the diagnosis. Interestingly 3 (5.0%) of these patients did in fact have AMI. Allowing for a degree of uncertainty, gestalt was recorded as "probably not" ACS in 493

(35.4%) of cases with 24 (4.9%) having AMI and 27 (5.5%) ACS. At the other end, clinicians perceived that the diagnosis was "definitely" ACS in a similarly small number of patients (59, 4.2%), with 37 (62.7%) having AMI and 42 (71.2%) ACS. Where clinicians deemed that the diagnosis was "probably" ACS (n=313, 22.5%), just over a quarter had AMI (n=84, 26.7%) and around one third had ACS (n=100, 32.0%).

The diagnostic accuracy of gestalt alone, and also combined with ECG and initial troponin, for "ruling out" ACS is shown in Table 3. In the cases where the clinician felt the diagnosis was "definitely not" ACS, the diagnostic accuracy was high with a sensitivity of 98.8% and negative predictive value (NPV) of 95.0%. If ACS had been "ruled out" in all cases where the clinician felt the diagnosis was either "definitely not" or "probably not" ACS, then sensitivity would have dropped to 87.8% and NPV to 94.8%. Interestingly, the diagnostic accuracy of gestalt as a "rule out" strategy was not substantially changed much by combining it with an ECG without ischemic features and an initial cardiac troponin concentration below the 99th percentile upper reference limit. The high accuracy of gestalt in the "definitely not" ACS group was improved to a sensitivity of 100.0% and an NPV of 100.0% when combined with ECG and troponin, but this "rule out" strategy would only have "ruled out" ACS in 55 (4.1%) patients.

The diagnostic accuracy of gestalt alone, and also combined with ECG and troponin, for ruling in ACS is shown in Table 4. Where the gestalt was "definitely" ACS, the diagnostic accuracy was high with a specificity of 98.5% and PPV of 71.2%. Interestingly, whilst the PPV increased to 95.0% and 94.1% when gestalt was combined with an ECG with ischaemic features and both an ECG with ischaemic features and an initially elevated troponin as a diagnostic strategy, the specificity decreased to 97.9% and 90.0% respectively. With lower levels of clinical certainty, the accuracy of "rule in" strategies dropped (Table 4).

Discussion

In this multi-center study we have robustly demonstrated that clinician gestalt alone is not sufficiently accurate or safe to either "rule in" or 'rule out' ACS as a clinical decision-making and management strategy in patients who the physician decided to proceed with an ACS evaluation. We prospectively evaluated clinicians' global diagnostic assessment or gestalt in a large cohort of undifferentiated patients with suspected cardiac chest pain. Gestalt has not been extensively studied but the limited evidence has suggested potential diagnostic value. In a single center prospective cohort study, the diagnostic accuracy of gestalt (low risk, intermediate risk or high risk) performed similarly to the HEART score.[18]

A previous single center prospective cohort study performed by our group found that gestalt, assessed in the same way, performed well. When combed with cardiac troponin, that study found that gestalt could be used to "rule out" ACS and discharge up to one quarter of patients who presented with suspected ACS with no missed AMI and a low incidence of 30-day MACE (0.9%).[17] In that study of 458 patients with suspected cardiac chest pain, 17.7% of whom had AMI, the area under the ROC curve for gestalt in diagnosing AMI was 0.76 (95% CI 0.70 – 0.82).[17] In our study of 1,391 patients with suspected cardiac chest pain, 14.9% of whom had AMI and 17.3% ACS, the area under the ROC curve for gestalt in diagnosing ACS is very similar at 0.75 (95% CI 0.72 to 0.79). The consistency suggests that the true diagnostic value lies around this mark.

The first key role which gestalt could play in decision-making and management is in "ruling out" ACS in order to discharge and avoid unnecessary admissions. Using gestalt alone, as a strategy to discharge patients, was less accurate than previously noted in the literature. In the

earlier single center study, discharging patients whom the clinician believed the diagnosis was "definitely not" or "probably not" ACS had a sensitivity of 95.1% (95% CI 87.8 - 98.6 and NPV of 96.8% (95% CI 92.0 - 99.1).[17] Our data showed that in the notably small number (4.4%) of patients whom the clinician felt the diagnosis was "definitely not" ACS, the sensitivity was high at 98.8% (95% CI 96.4 - 99.7) and NPV 95.0% (95% CI 85.7 - 98.4). Although these figures show that we are accurate, even at this highest "rule out" threshold, the post-test probability of missing ACS at 5% is too high risk for use in clinical practice. A survey of acceptable risk of MACE following discharge from the ED amongst Emergency Physicians showed that almost half of clinicians accepted a miss-rate of 1% or less with a majority accepting a miss-rate of 0.5% or less.[21] In this study gestalt alone, even at this highest threshold, did not achieve this. Discharging patients whom the clinician believed the diagnosis was "definitely not" or "probably not" ACS as per the earlier study had a comparatively lower sensitivity at 87.8% (95% CI 82.9 -91.8) and NPV 94.8% (95% CI 92.8 - 96.3%). Adding an ECG without ischemic features for a rule out strategy of gestalt and ECG performs similarly to gestalt alone and adding an initial troponin below the 99th centile is also insufficient. Adding criteria of a normal ECG and normal first troponin to gestalt "definitely not" made a very accurate diagnostic "rule out" strategy achieving a sensitively and NPV of 100%. However, this would only rule out ACS in 4.1% of patients and would thus have a minimal impact in clinical practice.

Prior to this study, the field was faced with the vital unanswered question about whether cardiac troponin testing is undertaken too often in the context of patients with possible ACS. Our multi-center study has clearly shown that gestalt cannot be reliably be used as a "rule out" strategy. When clinicians deemed that the diagnosis was "definitely not" ACS, they were incorrect on 5% of occasions. This suggests that it would be unsafe to reduce cardiac

troponin testing in this patient group. It is, however, crucial to emphasize that we only included patients with chest pain or discomfort where ACS was suspected (even if the treating clinician felt that the diagnosis was highly unlikely) with no other apparent cause. Our findings do not apply to patients who did not pass the clinicians pre-test probability threshold for warranting investigation for ACS. Our findings cannot be extrapolated to patients with other symptoms.

The second key role which gestalt could play in decision-making and management is in "ruling in" those with ACS to promptly treat and manage the condition. How should our clinical judgement impact our management strategy? Should we start treatment based on clinical suspicion whilst awaiting the serial troponin result? There is very little previous evidence on the accuracy of gestalt as a diagnostic "rule in" strategy. In the small number of patients (4.4%) where the treating clinician believed the patient "definitely" had ACS, there was a high level of accuracy with specificity 98.5% (95% CI 97.6 – 99.1), PPV 71.2% (95% CI 58.9 – 81.0) with a positive likelihood ratio of 12.1 (95% CI 7.01 - 20.87). When those whom the clinician felt "probably" had ACS are considered, which is 22.6% of patients, gestalt accuracy drops to having a specificity of 79.8% (95% CI 77.3 – 82.1), PPV of 37.7% (95% CI 34.1 – 41.5) and positive likelihood ratio of 3.0 (95% CI 2.53 - 3.47). This clearly isn't accurate enough to rule in ACS or consider treatments or interventions with considerable risk. It could however, help shape our communication with the patient, relatives and onward medical team and inform our decision making around administering anti-platelet therapy. Having an ECG with ischemic features and an initial troponin above the 99th percentile increase the PPV and positive likelihood ratio of a combined gestalt, ECG and troponin "rule in" strategy but only applied to <2% of patients and saw a drop in specificity.

Limitations

In this study, clinicians were not blinded to the ECG or initial cardiac troponin results. It was considered to be unethical to blind the clinician to these results given the potential for this to delay the identification and treatment of ACS. Our results cannot, therefore, truly assess the diagnostic accuracy of 'gestalt' in isolation. However, our method represents an entirely pragmatic evaluation of 'gestalt' in practice, where practicing clinicians also have access to this information. The accuracy of the clinician recording the presence of acute ischemic ECG features was not validated for this analysis; however this pragmatic approach also replicates a real world practice setting.

Conclusions

Our study confirms that, once a clinician has decided that a patient warrants investigation for a possible diagnosis of ACS, the gestalt of the clinician is insufficiently accurate to either "rule in" or "rule out" that diagnosis, even when they perceive that the diagnosis is present or absent with certainty. The findings give statistical evidence to what emergency physician clinical judgement represents from a probabilistic decision making perspective and can be used to advise patients, family and the medical professionals involved in on-going care.

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Figures

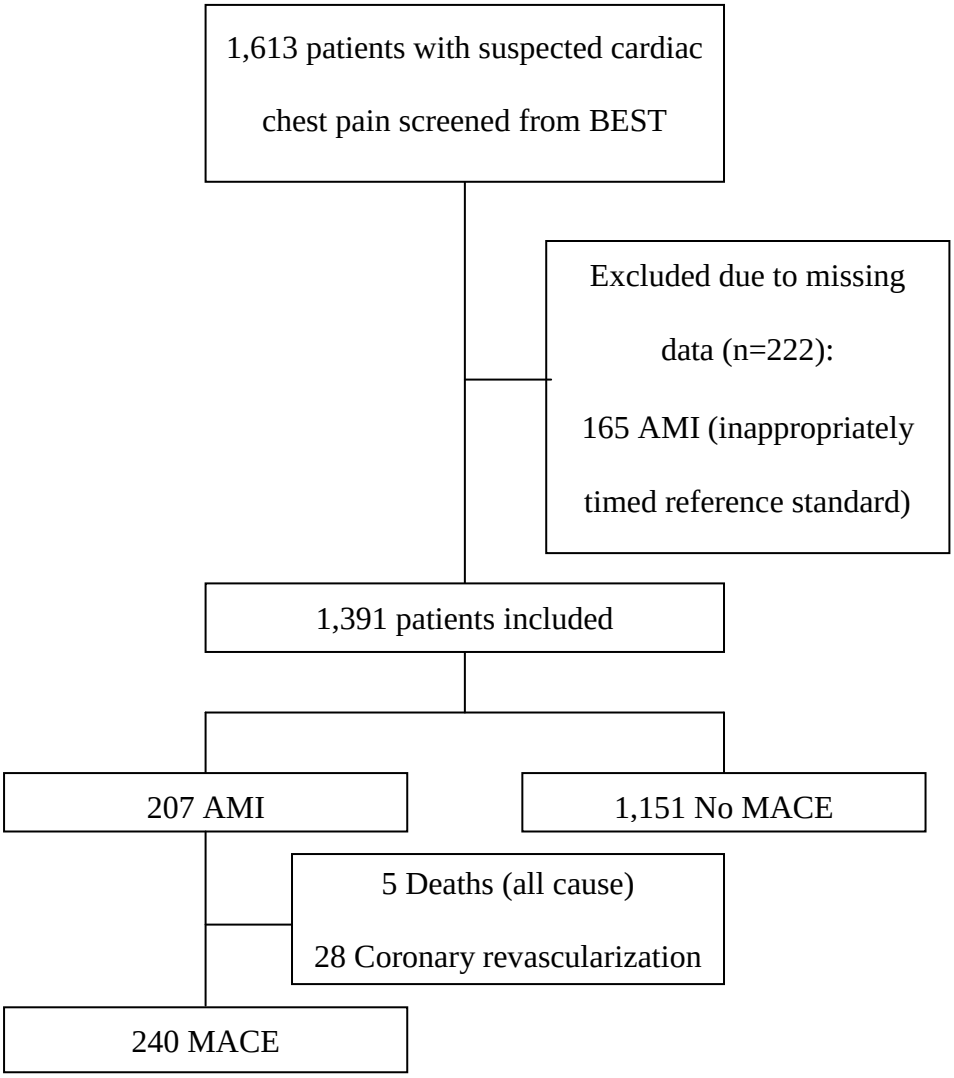

Figure 1

Flow diagram of enrolled and excluded

Table 1: Baseline characteristics and cardiovascular risk factors

Risk Factor	Present (%)	MACE (%)	Not present (%)	MACE (%)
Male	893 (64.2)	173 (19.4)	498 (35.8)	67 (13.5)
Hypertension	688 (49.5)	147 (21.4)	702 (50.5)	67 (13.5)
Hyperlipidaemia	523 (37.6)	114 (21.8)	855 (61.5)	93 (13.3)
Previous MI	387 (27.8)	91 (23.5)	1001 (72.0)	123 (14.4)
Previous angina	389 (28.0)	96 (24.7)	979 (70.5)	149 (14.9)
Diabetes Type 1	24 (1.7)	9 (37.5)	1359 (97.7)	142 (14.5)
Diabetes Type 2	267 (19.2)	68 (25.5)	1119 (80.5)	229 (16.9)
Current Smoker	273 (20.0)	55 (20.2)	1085 (79.7)	172 (15.4)

Table 2: Proportion of patients with AMI and ACS stratified by clinician gestalt

Gestalt Likert Scale	"Definitely not" ACS	"Probably not" ACS	"Could be" ACS	"Probably" ACS	"Definitely" ACS
Total number (%)	60 (4.3)	493 (35.4)	466 (33.5)	313 (22.5)	59 (4.3)
Number with AMI (%)	3 (5.0)	24 (4.9)	59 (12.7)	84 (26.8)	37 (62.7)
Number with ACS (%)	3 (5.0)	27 (5.5)	67 (14.4)	100 (32.0)	42 (71.2)

Table 3: Diagnostic accuracy of clinician gestalt for ACS "rule-out", both alone and in combination with the ECG and initial cardiac troponin concentration

Rule out strategy	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	NPV (%) (95% CI)	PPV (%) (95% CI)	Patients (%)
Clinician believes the diagnosis is "definitely not" ACS	98.8 (96.4 - 99.7)	5.1 (3.9 - 6.5)	95.0 (85.7 - 98.4)	18.2 (17.9 - 18.4)	60 (4.4)
Clinician believes the diagnosis is "definitely not" or "probably not" ACS	87.8 (82.9 -91.8)	45.5 (42.5 - 48.4)	94.8 (92.8 - 96.3)	24.8 (23.4 - 26.1)	480 (35.4)
Clinician believes the diagnosis is "definitely not" ACS + ECG[§]	98.3 (95.2 - 99.7)	5.2 (3.9 - 6.7)	94.9 (85.5 - 98.3)	14.8 (14.5 - 15.1)	59 (4.4)
Clinician believes the diagnosis is "definitely not" or "probably not" ACS + ECG[§]	86.1 (80.2 - 90.8)	46.3 (43.3 - 49.4)	95.2 (93.3 - 96.7)	21.1 (19.8 - 22.5)	466 (34.4)
Clinician believes the diagnosis is "definitely not" ACS + ECG + troponin[¶]	100.0 (88.1 - 100.0)	5.9 (4.4 - 7.6)	100.0	3.2 (3.1 - 3.2)	55 (4.1)
Clinician believes the diagnosis is "definitely not" or "probably not" ACS +ECG + Troponin[¶]	86.2 (68.4 - 96.1)	50.0 (46.7 - 53.2	99.2 (97.9 - 99.7)	5.1 (4.3 - 5.9)	418 (30.8)

[§]Gestalt combined with an ECG with no ischemic features to "rule-out" ACS

[¶]Gestalt combined with an ECG with no ischemic features and an initial troponin <99th Centile (normal) to "rule-out" ACS

Table 4: Diagnostic accuracy of clinician gestalt for ACS "rule in", both alone and in combination with the ECG and initial cardiac troponin concentration

Rule in strategy	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	NPV (%) (95% CI)	PPV (%) (95% CI)	Patients (%)
Clinician believes the diagnosis is "Definitely" ACS	18.3 (13.5 - 23.9)	98.5 (97.6 – 99.1)	85.5 (84.7 - 86.3)	71.2 (58.9 – 81.0)	59 (4.4)
Clinician believes the diagnosis is "Probably" or "Definitely" ACS	60.0 (53.4 - 66.4)	79.8 (77.3 – 82.1)	90.7 (89.3 - 91.9)	37.7 (34.1 – 41.5)	307 (22.6)
Clinician believes the diagnosis is "Definitely" ACS + ECG[§]	38.0 (24.7 - 52.8)	97.9 (88.7 – 100.0)	59.7 (54.3 - 64.9)	95.0 (72.6 – 99.3)	20 (1.5)
Clinician believes the diagnosis is "Probably" or "Definitely" ACS + ECG[§]	86.0 (73.3 - 94.2)	44.7 (30.2 – 59.9)	75.0 (58.5 - 86.5)	62.3 (55.6 – 68.7)	49 (3.6)
Clinician believes the diagnosis is "Definitely" ACS + ECG + Troponin[¶]	39.0 (24.2 - 55.5)	90.0 (55.5 – 99.8)	26.5 (20.7 - 33.2)	94.1 (70.6 – 99.1)	17 (1.3)
Clinician believes the diagnosis is "Probably" or "Definitely" ACS + ECG + Troponin[¶]	87.8 (73.8 - 95.9)	50.0 (18.7 – 81.3)	50.0 (26.3 - 73.7)	87.8 (79.3 – 93.1)	24 (1.8)

[§]Gestalt combined with an ECG with ischemic features to "rule in" ACS

[¶]Gestalt combined with an ECG with ischemic features and an initial troponin >99th Centile (elevated) to "rule in" ACS