救急外来での診断演習：感度、特異度、そして尤度比

救急外来での診断演習　感度・特異度・そして尤度比の活用方法を知る

目的

鑑別診断手順を整理する

目標

感度、特異度の意味をおさらいする

尤度比の使い方を確認する

このセミナーを終えるとあなたは

- 感度の高い検査、特異度の高い検査が、確定診断や除外診断にどう役立つのか説明できるようになる
- 尤度比の求め方を説明できる
- 尤度比を使うノモグラムが使えるようになる

セクション１：救急外来を想像してみよう

まず質問１

病院の救急外来を受診する患者を考えてみましょう。

どんな症状を訴える来院患者が多いでしょうか。

以下の主訴の患者が占める割合をちょっと考えてみましょう。

発熱	（　%）	腹痛・腹部症状	（　%）
胸痛・胸部症状	（　%）	頭痛・頭部症状	（　%）
けが・外傷	（　%）	意識障害	（　%）

他に頻度の多いと思う主訴は何がありますか ＿＿＿＿＿＿＿＿＿＿

質問２

あなたの救急外来に、「胸部症状」「胸痛」を訴えて来院する患者の最終診断はどんなものがありますか。以下に列挙してみましょう。少なくとも３つ以上。目標５つ以上。できれば、１０個以上。

EBOnCallの記述 http://www.eboncall.org

Chest pain

Causes

Common causes of chest pain include [c]

1) myocardial infarction
2) angina
3) pulmonary embolism
4) chest infection
5) musculoskeletal pain
6) pericarditis

Rarer causes include [d]

1) aortic dissection
2) oesophageal spasm

Note:

One in six patients with anterior or left-sided chest pain have a myocardial infarction (14% to 20%) [a]

The risk is higher in elderly patients (20%: 95% CI: 19% to 22%) [a] and patients with a typical history [a]

One in four patients anterior or left-sided chest pain have unstable angina (24%: 95% CI: 21% to 27%) [a] - the risk is higher in elderly patients (44%: 95% CI: 42% to 45%) [a]

Myocardial infarction, angina and pulmonary embolism are common causes of chest pain

Chest pain in emergency departments [a] [c]	% (95% CI)
myocardial infarction	17% (14% to 20%)
unstable angina	24% (21% to 27%)
stable angina	9.0% (5.6% to 12%)
pulmonary embolism	5.8% (3.0% to 8.5%)
other pulmonary disease	5.8% (3.0% to 8.5%)
chest wall pain	5.4% (2.7% to 8.1%)
pericarditis	5.0% (2.5% to 7.6%)
psychogenic	2.9% (0.9% to 4.8%)
other heart disease	1.1% (0.0% to 2.3%)
other disease	1.1% (0.0% to 2.3%)
unknown	11% (7.5% to 15%)

Only 40% of cases or aortic dissection are diagnosed following history, physical, ECG and CXR. (14% mistaken for ischaemic heart disease, 14% for other aortic disease, 7% heart failure) [c]

できれば、鑑別診断のリストアップの時に、その疾患の確率まで予測できると次のステップに進みやすい。
もちろん、おおざっぱでよい。

力試しあなたの救急外来に受診した「2時間続く胸痛・胸部症状」を主訴とした患者が急性心筋梗塞あるいは不安定狭心症である確率をおおざっぱに見積もろう

あなたの予測する確率：＿＿＿％

以下に示す要因があった場合に、その確率はどうなるだろうか。予測してみよう。もちろん、おおざっぱに。

要因１：年齢

	あなたの予測する確率	あなたの尤度比
その患者の年齢が２７才だったら		
その患者の年齢が４５才だったら		
その患者の年齢が６５才だったら		
その患者の年齢が８５才だったら		

要因２：性別

	あなたの予測する確率	あなたの尤度比
その患者が男性だったら		
その患者が女性だったら		

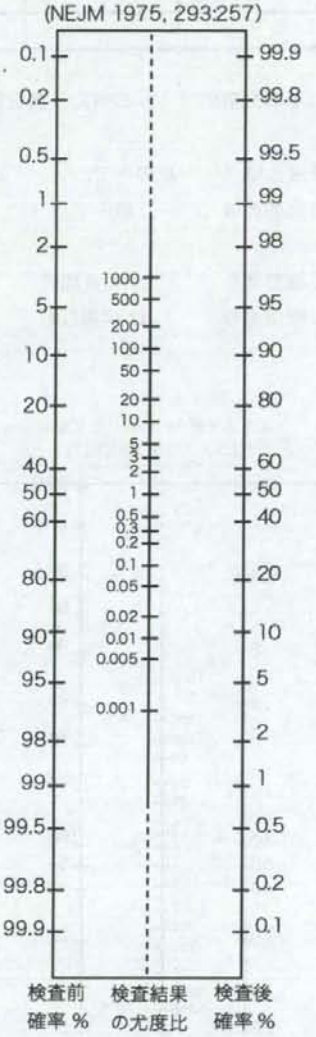
要因３：症状

	あなたの予測する確率	あなたの尤度比
「胸が圧迫される」「押される」		
「左を下にすると痛む」		
「息をすると痛む」		
痛みを訴える場所に圧痛がある		
左肩から腕も痛む		
右肩から腕も痛む		

要因４：検査結果

	あなたの予測する確率	あなたの尤度比
連続する２誘導でST上昇がある		
心電図は正常である		
白血球数が12000/mm3である		
血清トロポニン値が上昇していない		

尤度比を使うためのノモグラム
(NEJM 1975, 293:257)



確認作業：あなたの所見の重み付けを見積もる

配布したハンドカード、あるいは上記のノモグラムを用いて、それぞれの所見のあなたの重み付けを求めてみよう。

重み付けは、「尤度比（ゆうどひ）：Likelihood Ratio」という値で求められる。

求め方：まずあなたが最初に見積もった確率を左端のライン上にマークする。次に、その所見によって変わった確率を右端のラインのマークし、その二つの点を結んだ線と中央の線との交点が、その所見の尤度比である。

たとえば、あなたが最初の確率を１０％だと見積もっていて、患者が２７才だったらその確率が２％になると考えた場合、右端の１０という点から、右端の２という点まで結んで線を書くと中央の線と０．２あたりで交わる。これが、あなたの見積もった尤度比である。

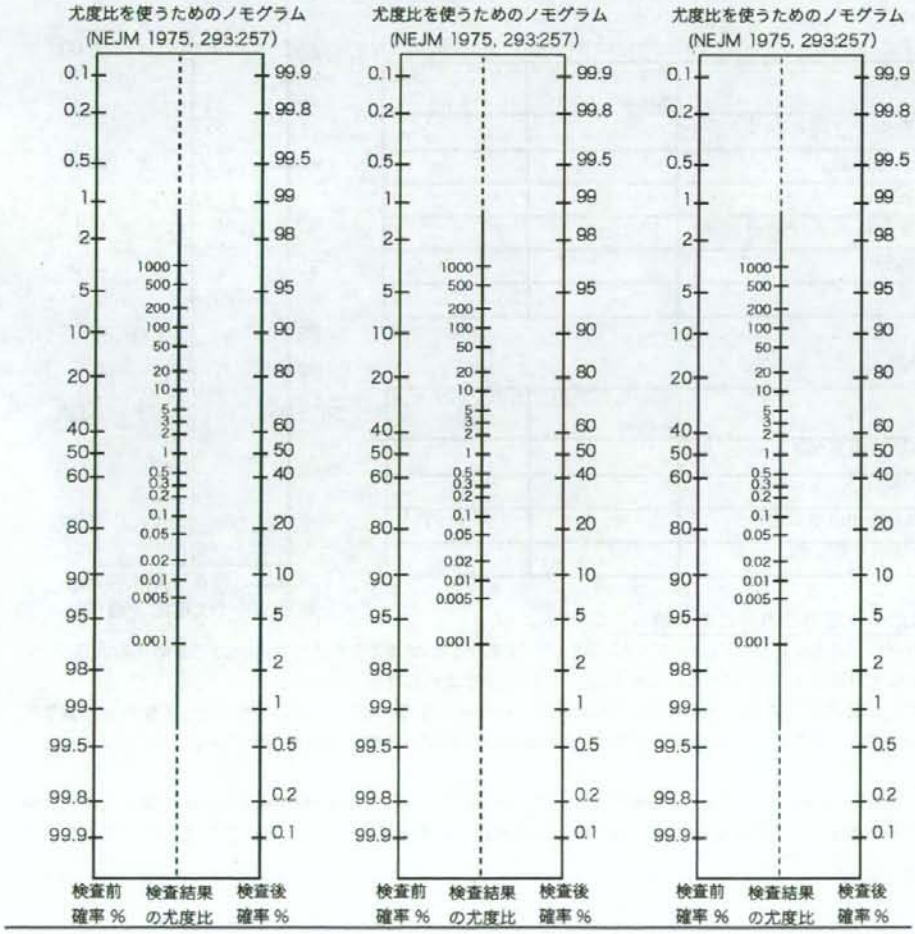
感度と特異度もおさらいしておこう

	疾患あり	疾患なし	
検査陽性			
検査陰性			

以下の文章の（ ）の中に、選択肢A-Dのうちからもっとも適切なものを一つずつ選んで記入せよ

感度とは（ ）の中で、（ ）の占める割合である
特異度とは（ ）の中で、（ ）の占める割合である

A 検査陽性　　B 検査陰性
C 疾患あり　　D 疾患なし



診断の指標の使い方：感度、特異度、そして尤度比（ゆうどひ）

感度と特異度

	疾患あり	疾患なし
検査陽性	a	b
検査陰性	c	d

感度 a/(a+c)、　**特異度** d/(b+d)

大まかな憶え方：

感度が高い検査→偽陰性がほとんどない。従って陰性だったらその疾患の除外診断に役立つ。

特異度の高い検査→偽陽性がほとんどない。従って陽性だったらその疾患の確定診断に役立つ。

尤度比（ゆうどひ）の求め方

まず、感度と特異度を用いて２×２表を埋める。横方向に疾患あり/疾患なしを求めると尤度比が得られる。

	疾患あり	疾患なし	尤度比
検査陽性	感度	1−特異度	感度/（1−特異度）
検査陰性	1−感度	特異度	（1−感度）/特異度

例：感度95%　特異度90%の検査であれば以下のようになる。

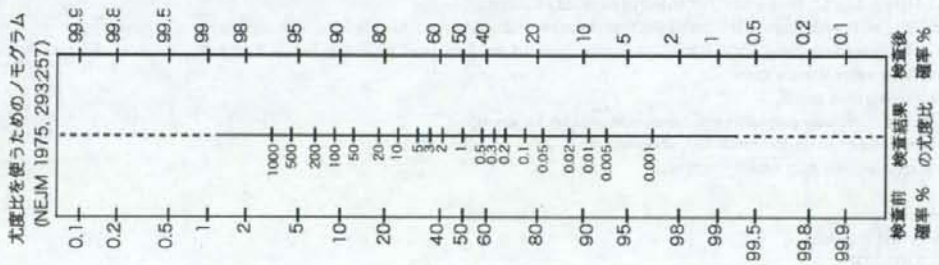
	疾患あり	疾患なし	尤度比
検査陽性	95	10	95/10=9.5
検査陰性	5	90	5/90=0.056

検査陽性の尤度比9.5、検査陰性の尤度比0.056

感度90%　特異度10%の検査（疾患があろうがなかろうが90%の確率で陽性になる、無意味な検査）であれば以下のようになる。

	疾患あり	疾患なし	尤度比
検査陽性	90	90	90/90=1
検査陰性	10	10	10/10=1

いずれの尤度比も１．つまり、どちらの検査結果であっても確率に影響を与えないことを示している。



EB OnCallのインターネットサイトに示されているCAT (Critical Appraised Topic)の例

Chest pain: clinical features and ECG helped in the initial diagnosis but cardiac enzymes did not.
Clinical bottom line (level 1b)

1. Roughly 40% of patients with chest pain had unstable angina or a myocardial infarction.
2. In patients with chest pain, unstable angina or MI was more likely if
   * previous history of MI (LR+2.3)
   * pain described as a pressure (LR+1.7)
   * male (LR-1.3)
   * increasing age
   * ECG indicating probable MI (LR+8.7)
   * ECG indicating ischemia or strain not known to be old (LR+3.1)
3. Unstable angina or MI was less likely if
   * sharp or stabbing pain (LR+0.41)
   * no previous history of MI or angina (LR-0.37)
   * pain pleuritic, positional or reproduced on palpation (LR+0.13)

   (Patients with all three are unlikely to have MI or unstable angina)
4. Traditional 'cardiac enzymes' taken in the emergency department were not very helpful. AST is most helpful at diagnosing or excluding MI if taken > 12 hours after the onset of chest pain.

Lee et al: Archives of Internal Medicine 1985; 145: 65-69 Expires March 2003

The study
Setting: emergency department, university hospital, USA
596 patients (aged mean 56 years, 52% female) anterior, precordial or left-sided chest pain
Excluded if
* <25
* not willing to return in 48-72 hours for repeat ECG and cardiac enzymes
* local trauma
* abnormal chest X-ray

Independent blinded reference standard, applied in all patients from a consecutive appropriate spectrum.
Reference standard:
* MI if any of
  - o AST > twice upper limit of normal, which then returned to normal. No intramuscular injection, muscle trauma or hepatic disease
  - o CK-MB > 5% total CK
  - o LDH1 > LDH2. No haemolytic anaemia or renal infarction
  - o ECG - new pathological q waves (> 40 ms duration and > 25% decrease in amplitude of following R wave)
  - o scintiscan showing focal uptake in cardiac area; if enzyme peak occurred before hospital admission and patient had no previous MI or valve calcification

  unstable angina if any of
  - o senior clinician's diagnosis not contraindicated by follow-up
  - o abnormal exercise tolerance test, abnormal angiogram or follow-up history
  - o known angina pain which worsened

Diagnostic test:
* history and physical
* CK, AST, LDH

The evidence
pre-test probability of MI: 17%, (95% CI: 14% to 21%)
pre-test probability of unstable angina: 24%, (95% CI: 21% to 27%) つまりMIかUAPの確率の集計は40%程度

	MI or UAP	no MI or UAP	LR(95% CI)	post-test probability
aged 80+	25	14	3.53(1.94 to 6.42)	71%
aged 70-79	43	28	2.17(1.39 to 3.39)	61%
aged 60-69	75	60	1.77(1.31 to 2.38)	56%
aged 50-59	56	70	1.13(0.83 to 1.54)	44%
aged 40-49	31	88	0.50(0.34 to 0.72)	26%
aged 30-39	5	61	0.12(0.047 to 0.28)	8%
aged 25-29	2	28	0.10(0.024 to 0.42)	7%
total	247	349		

＜中略＞

diagnostic test	MI or UAP	no MI or UAP	LR+(95% CI)	post-test probability	LR-(95% CI)	post-test probability
male	135	151	1.3(1.1 to 1.5)	47%	0.80(0.68 to 0.94)	36%
pressure	137	116	1.7(1.4 to 2.0)	54%	0.67(0.57 to 0.78)	32%
aching	25	54	0.65(0.42 to 1.0)	32%	1.1(1.0 to 1.1)	43%
burning/ indigestion	19	24	1.1(0.63 to 2.0)	44%	0.99(0.95 to 1.0)	41%
sharp or stabbing	35	122	0.41(0.29 to 0.57)	22%	1.3(1.2 to 1.5)	48%
other	31	33	1.3(0.84 to 2.1)	48%	0.97(0.91 to 1.0)	41%
history of MI or angina	184	115	2.3(1.9 to 2.7)	62%	0.38(0.30 to 0.48)	21%
pain pleuritic, positional or reproduced by palpation	13	138	0.13(0.077 to 0.23)	9%	1.6(1.4 to 1.7)	53%
total	247	349				

diagnostic test	MI or UAP	no MI or UAP	LR(95% CI)	post-test probability
pleuritic pain	0	36	0.0(0.0 to 0.12)	0%
partly pleuritic pain	13	83	0.22(0.13 to 0.39)	14%
pain not pleuritic	234	230	1.4(1.3 to 1.6)	50%
total	247	349		

diagnostic test	MI or UAP	no MI or UAP	LR(95% CI)	post-test probability
positional pain	2	22	0.13(0.03 to 0.54)	8%
pain partly positional	20	92	0.31(0.19 to 0.48)	18%
pain not positional	225	235	1.4(1.3 to 1.5)	49%
total	247	349		

diagnostic test	MI or UAP	no MI or UAP	LR(95% CI)	post-test probability
pain reproduced by chest wall palpation	9	115	0.11(0.057 to 0.21)	7%
pain partially reproduced by chest wall palpation	8	26	0.43(0.20 to 0.94)	24%
pain not reproduced by chest wall palpation	230	208	1.6(1.4 to 1.7)	53%
total	247	349		

diagnostic test	MI	no MI	LR(95% CI)	post-test probability
AST level in patients with chest pain onset >12 hours ago: 100	0.30	0.01	30	89%
80	0.09	0.04	2.3	39%
60	0.28	0.05	5.6	60%
50	0.02	0.05	0.40	10%
40	0.13	0.22	0.59	14%
30	0.12	0.37	0.32	8%
<30	0.02	0.26	0.078	2%

diagnostic test	MI	no MI	LR(95% CI)	post-test probability
AST level in patients with chest pain onset <12 hours ago: 100	0.07	0.03	2.3	39%
80	0.05	0.03	1.7	32%
60	0.11	0.03	3.7	50%
50	0.13	0.04	3.3	47%
40	0.16	0.26	0.62	14%
30	0.29	0.39	0.74	17%
<30	0.19	0.22	0.86	19%

* Data for the final two tables was obtained from ROC curves.

Comments

1. CK was found to be unhelpful in diagnosing MI if patients attended >12 hours after the onset of chest pain.
2. The study was performed before CK-MB was introduced- this is a helpful test at <12 hours.

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Myocardial infarction: ST elevation in 2 contiguous leads on the initial ECG diagnosed it

Clinical bottom line (level 2b)

1. One in six patients presenting to an emergency department with central or left-sided chest pain had a myocardial infarction.
2. ST elevation in 2 contiguous leads on the initial ECG diagnosed a myocardial infarction (LR+61) .
3. An elevated total CK (LR+6.0) , elevated leukocyte count (LR+6.8) or a decreased relative lymphocyte percentage (LR +6.3) made a myocardial infarction more likely but were not diagnostic.

Thomsen et al: Annals of Internal Medicine 1995; (122): 335-341 Expires March 2003

The study
Setting: emergency department, university hospital, USA
384 patients (aged , % male) presenting with anterior or left lateral chest pain

Excluded if
* insufficient data to exclude MI
* failed to return after 24 hours for repeat blood tests
* infection in the previous week
* exogenous glucocorticoid use in the previous month
* malignancy in previous 5 years
* transferred from another hospital
* major trauma, major gastrointestinal bleeding, surgery, dialysis or resuscitation in the previous week
* aged < 20

Independent blinded reference standard, applied in all patients from a non-consecutive appropriate spectrum.
Reference standard:
* one of
  - o CK-MB level > 9.6 mg/dl within 48 hours
  - o sudden unexplained death within 72 hours

Diagnostic test:
* ECG: ST elevation 1 mm or more in 2 contiguous leads
* creatine kinase
* leukocyte count

The evidence
pre-test probability of myocardial infarction: 18%, (95% CI: 14% to 22%)

diagnostic test	MI	no MI	LR+(95% CI)	post-test probability	LR-(95% CI)	post-test probability
positive ECG	27	2	62(15 to 250)	93%	0.61(0.51 to 0.74)	12%
elevated creatine kinase	29	22	6.0(3.7 to 9.8)	57%	0.62(0.50 to 0.76)	12%
elevated leukocyte count	33	22	6.8(4.3 to 11)	60%	0.56(0.45 to 0.70)	11%
decreased relative lymphocyte percentage	40	29	6.3(4.2 to 9.4)	58%	0.46(0.35 to 0.61)	9%
total	69	315				

Comments

1. The study also reported elevated rapid CK-MB levels, but since CK-MB is included in the reference standard the test characteristics are inaccurate.

鑑別診断を進めるときの原則

「1つの選択肢の確率は0から1まで（0%から100%まで）の値である」
「すべての選択肢の確率の合計は1（100%）である」

従って　鑑別診断名が1つしか思い浮かばなければ、それは「確定診断」になってしまう。

救急外来で鑑別を効率よく行う手順の一例
1）とりあえず、5つ、できれば10くらいの診断名（なるべく病態ではなく、診断名を考慮すること）をリストアップする。
2）次に、その中で頻度、重要度、緊急度を考慮して3つくらいの疾患に絞る。
3）その疾患に関して、確定診断に役立つ検査結果や除外診断に役立つ検査結果を求めて問診や身体所見を取り、検査計画を立て検査結果を読む。
4）もし、その3つのうち除外されるものがでたら、一番最初のリストから最も重要と思われるものを加えて、また3つのリストにする。
5）3）-4）の手順を繰り返す。確定診断が得られたらそこで終了。重要な疾患が除外され、緊急性が高くないと判断されれば、救急外来から返す。重要な疾患が除外されず緊急を要する可能性が残ると判断されれば、a)一旦入院、b)しばらく救急外来で様子を見る、c)重要な疾患の可能性が残ること、状態が変わればすぐ来院することを指示して帰宅させる　といったオプションを考慮する。

非常に感度の高い検査結果が陰性であれば、まず診断は否定されるし（SnNout）、非常に特異度の高い検査結果が陽性であれば診断は確実なものになる（SpPin）。
語呂合わせ：　Sensitivityの高い検査がNegativeだったらRule-Out
　　Specificityの高い検査がPositiveだったらRule-In
従って、その検査結果も陽性だったら意味があるか、陰性だったら意味かを、ちゃんと憶えておくことが重要になる。
注意点：感度と特異度はペアで知っておいて意味がある。例えば、「感度90%で特異度10%の検査」は診断する力はまったくない。よく考えてみれば、この検査は病気があろうがなかろうが、どっちにしても90%の確率で陽性になる検査である。感度が特異度の一方が良くても、もう一方がわるければその診断力を大きく損なってしまう。

尤度比（ゆうどひ：likelihood ratio）は感度と特異度から求められ、検査結果からより客観的に疾患の可能性を予測するのに有用な概念である。

診断の問いかけの具体例と課題
実際の診療の現場での診断検査治療の過程は、仮説（hypothesis）と問いかけ（questions）をもとに進められる。

仮説1：この患者は労作性狭心症だ。
問いかけ1：診断を確かめるために運動負荷心電図は行なうべきだろうか？
仮説2：この患者は急性硬膜下血腫ではない。
問いかけ2：この除外診断のために、頭部CTをとるべきだろうか？

最初に疑わしいと考えた診断にとらわれて、臨床所見や検査所見をその診断に都合の良いように判断し、考えた診断に対してさほど重要でない検査を繰り返すと、真の診断にたどり着けない危険は高くなる。

解説2：診断のための感度特異度の利用法・尤度比の説明、条件付き確率の考え方（感度・特異度を越えて）

ある疾患の疑われる患者にある検査を行なった。この検査は感度が90%、特異度が80%であった。検査前のこの疾患の可能性は10%程度と考えられた。この検査が陽性であった場合にはこの患者の疾患の可能性はどの程度と予想されるか。また、逆に陰性であった場合にはどの程度であると考えられるか。

考え方：

まず、感度が90%で特異度が80%の検査とはどんな検査であろうか。2分割表で考えると以下のようになる。

	疾患あり	疾患なし
検査陽性	0.9	0.2
検査陰性	0.1	0.8

考えやすくするために、この疾患の確率が10%の患者が100人いたとしよう。疾患ありの患者数は10人、疾患なしの患者数は90人となり、この数字から上記の2分割表を埋めると以下のようになる。

	疾患あり	疾患なし	
検査陽性	9	18	27
検査陰性	1	72	73
患者数	10	90	100

ここから、検査陽性のときの疾患ありの確率は9/27から1/3となる。陰性である場合には1/73から1.4%となる。

補足問題

この疾患の確率が50%の患者がいたとすると、この表は以下のようになる。

	疾患あり	疾患なし	
検査陽性	45	10	55
検査陰性	5	40	45
患者数	50	50	100

ここから、検査陽性のときの疾患ありの確率は45/55から約82%となる。陰性である場合には5/45から約11%となる。

今度は、この疾患の確率が90%の患者がいたとしよう。この場合は以下のようになる。

	疾患あり	疾患なし	
検査陽性	81	2	83
検査陰性	9	8	17
患者数	90	10	100

ここから、検査陽性のときの疾患ありの確率は81/83から約98%となる。陰性である場合には9/17から約53%となる。

このように、検査前のその患者の疾患である確率が、検査の陽性陰性の意味付けをかなり変えてしまう。たとえ検査としては十分容認できるであろう感度90%、特異度80%という検査であっても、検査前の確率が低ければその疾患であるという決定的な診断根拠にならず、検査前の確率が高い場合には検査が陰性であってもその疾患を否定することはできない。

もう一度、この表を見なおし、確率で書き直してみよう。まず、感度をsens特異度をspecとして表を書き直してみよう。

	疾患あり	疾患なし
検査陽性	sens	1−spec
検査陰性	1−sens	spec

検査前の疾患の確率をpとすると、疾患でない確率は1−pとなる。これに基づいて先程と同様の手順で表を完成させると以下のようになる。

	疾患あり	疾患なし
検査陽性	sens×p	(1−spec)×(1−p)
検査陰性	(1−sens)×p	spec×(1−p)
確率	p	1−p

ここから、検査陽性の場合の疾患のある確率は

sens×p/((1−spec)×(1−p)+ sens×p)

また、検査陰性の場合の疾患のある確率は

(1−sens)×p/((1−sens)×p+ spec×(1−p))

このように確率の計算式はかなり複雑になる。ここでオッズという考え方を用いると計算式は簡単になる。オッズとはある事象が起きる確率と起きない確率の比で表したものである。この患者の検査前のオッズはp：(1−p)となる。検査が陽性であった場合のこのオッズの変化は表から以下のように表すことができる。

検査が陽性であった場合のオッズ=検査前のオッズ×sens/(1−spec)←検査陽性の尤度比

検査が陰性であった場合のオッズ=検査前のオッズ×spec/(1−sens)←検査陰性の尤度比

確率（p）からオッズ（Odds）へ：Odds=p/(1-p)

オッズから確率へ：p=Odds/(1+Odds)

50%の確率のオッズは1．確率は0から1までの値をとり、オッズは0から無限大までの値をとる

先の例では検査陽性の尤度比は0.9/0.2から4.5、検査陰性の尤度比は0.1/0.8から0.125となる。もしも、疾患の確率が50%の患者を想定すると、オッズは50%/50%から1となる。この患者の検査が陽性であれば、1×4.5から、検査後のオッズは4.5となり、4.5/（1+4.5）から約82%となる。陰性であれば、検査後オッズは0.125となり、0.125/（1+0.125）から約11%となる。←当然のことながら、先の計算結果と同様となる。（この計算をしないで済むのが、参考資料のノモグラムを用いた手順である。）

Bedside Diagnosis of Coronary Artery Disease: A Systematic Review

Andrea Akita Chun, MD, Steven R. McGee, MD

PURPOSE: To assess the accuracy of bedside findings for diagnosing coronary artery disease and acute myocardial infarction.
METHODS: A MEDLINE search was performed to retrieve articles published from January 1966 to January 2003 that were relevant to the bedside diagnosis of coronary disease in adults.
RESULTS: In patients with stable, intermittent chest pain, the most useful bedside predictors for a diagnosis of coronary disease were found to be the presence of typical angina (likelihood ratio [LR] = 5.8; 95% confidence interval [CI]: 4.2 to 7.8), serum cholesterol level >300 mg/dL (LR = 4.0; 95% CI: 2.5 to 6.3), history of prior myocardial infarction (LR = 3.8; 95% CI: 2.1 to 6.8), and age >70 years (LR = 2.6; 95% CI: 1.8 to 4.0). Nonanginal chest pain (LR = 0.1; 95% CI: 0.1 to 0.2), pain duration >30 minutes (LR = 0.1; 95% CI: 0.0 to 0.9), and intermittent dysphagia (LR = 0.2; 95% CI: 0.1 to 0.8) argued against a diagnosis of coronary disease. In patients with acute chest pain, the most important bedside predictors for a diagnosis of myocardial infarction were new ST elevation (LR = 22; 95% CI: 16 to 30), new Q waves (LR = 22; 95% CI: 7.6 to 62), and new ST depression (LR = 4.5; 95% CI: 3.6 to 5.6). A normal electrocardiogram (LR = 0.2; 95% CI: 0.1 to 0.3), chest wall tenderness (LR = 0.3; 95% CI: 0.2 to 0.4), and pain that was pleuritic (LR = 0.2; 95% CI: 0.2 to 0.3), sharp (LR = 0.3; 95% CI: 0.2 to 0.5), or positional (LR = 0.3; 95% CI: 0.2 to 0.5) argued against the diagnosis of myocardial infarction.
CONCLUSION: The accuracy of bedside predictors depends on the clinical setting. In the evaluation of stable, intermittent chest pain, a patient's description of pain was found to be the most important predictor of underlying coronary disease. In the evaluation of acute chest pain, the electrocardiogram was the most useful bedside predictor for a diagnosis of myocardial infarction. Aside from the extremes in cholesterol values, the analysis of traditional risk factors changed the probability of coronary disease or myocardial infarction very little or not at all. **Am J Med. 2004;117:334–343.**

Ever since William Heberden's original description of angina in 1768 (1), clinicians have regarded chest pain as the principal and often sole diagnostic clue to coronary artery disease. Coronary artery disease is the leading cause of death in the United States, responsible for 700,000 deaths per year (2). Chest pain accounts for up to 10% of acute complaints evaluated in internal medicine clinics (3) and up to 8% of all visits to emergency departments (4,5).

Despite the prevalence of chest pain and coronary artery disease, diagnosis is often difficult. More than 80% of patients presenting to clinics with chest pain receive additional diagnostic testing, yet only a minority have coronary artery disease eventually confirmed (3). About half of patients with acute chest pain in emergency departments are admitted with possible ischemia, yet only 1 in 3 have myocardial infarction established later (6,7). Moreover, despite this conservative admission policy to coronary care units, 1% to 8% of all patients with myocardial infarction, as confirmed by cardiac enzyme measurements, are misdiagnosed and discharged home (6,8–12).

The purpose of this paper was to assess the accuracy of bedside findings for diagnosing coronary artery disease and acute myocardial infarction. Bedside findings are defined as the patient interview, risk factor analysis, physical examination, and electrocardiogram (ECG). We compared the value of these bedside findings in the evaluation of stable, intermittent chest pain with their value in the evaluation of acute chest pain.

METHODS

Using MEDLINE (January 1966 to January 2003), one author (AAC) performed the following search strategy, limited to English-language publications and human subjects, to retrieve all relevant publications on the bedside diagnosis of coronary artery disease in adults. The following Medical Subject Heading terms were combined with the terms *coronary disease/diagnosis* and *myocardial infarction/diagnosis*: *chest pain/diagnosis*, *electrocardiography*, *risk factors*, *physical examination*, and *medical history taking*. A text word search combining *coronary artery*

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Manuscript submitted October 15, 2003; and accepted in revised form March 2, 2004.

0002-9343/04/$–see front matter
doi:10.1016/j.amjmed.2004.03.021

Table 1. Definition of Findings

Finding (References)	Definition
Patient Interview	
Typical angina (13–20)	Substernal discomfort, precipitated by exertion, improved with rest or nitroglycerin (or both) in less than 10 minutes (many patients also report radiation to shoulders, jaw, or inner arm).
Atypical angina (13,14,16,19,20)	Substernal discomfort with atypical features; nitroglycerin not always effective; inconsistent precipitating factors, relieved after 15 to 20 minutes of rest.
Nonanginal chest pain (13,14,16,19,20)	Pain unrelated to activity, unrelieved by nitroglycerin, otherwise not suggestive of angina.
Angina reproducibility score = 10 (21,22)	When asked "if you go up a hill on 10 separate occasions, on how many of these do you experience chest pain?", the patient answers "10".
Angina scale (21,22)	The clinician scores 1 point for each of the following findings: reproducibility score = 10 (see above); the patient answers "0" or "1" when asked the question "If you have the pain 10 times in a row, how many times does it occur when you are resting or sitting quietly?"; the patient's pain lasts less than 5 minutes.
Physical Examination	
Earlobe crease (23–27)	Deep diagonal crease across the lower ear lobe, from the lower portion of the tragus to the edge of the lobe.
Arcus senilis (28)	Grey-white circular deposits in the periphery of the cornea.
Ankle-brachial index (29)	The highest systolic blood pressure in the posterior tibial or dorsalis pedis artery divided by systolic blood pressure in the brachial artery (using a Doppler stethoscope after the patient has been positioned supine for at least 5 minutes).
Risk Classification for Predicting Serious Complications	
High risk (30–31)	ECG reveals new ST elevation or Q waves; or ECG reveals new ST depression or T-wave inversion and the patient has two or more risk factors.*
Moderate/low risk (30–31)	Not meeting criteria for high or very low risk.
Very low risk (30–32)	ECG lacks ST-T-wave changes and Q waves, and the patient lacks risk factors*

* Risk factors = systolic blood pressure <110 mm Hg; rales heard above the bases bilaterally; chest pain that is worse than prior angina or the same as prior myocardial infarction, or pain that occurs in the postinfarction or postrevascularization setting.
ECG = electrocardiogram.

disease and *myocardial infarction* with the following terms was also used: *likelihood* and *history, physical examination, risk factors, arcus senilis, earlobe crease, ankle-brachial index, electrocardiogram, atypical chest pain*, and *GI cocktail*. The search tool "all related articles" and the bibliographies of selected articles were consulted to obtain further citations.

Both authors independently reviewed all relevant articles and included those that satisfied the following four criteria: the study enrolled patients presenting to clinicians with symptoms suggestive of coronary artery disease; the clinical findings were clearly defined (Table 1); there was an independent comparison of the bedside finding with an accepted diagnostic standard; and the study included enough information to calculate sensitivity, specificity, and likelihood ratios. For coronary artery disease, the diagnostic standard was cardiac catheterization revealing substantial stenosis of any major epicardial vessel. For myocardial infarction, the diagnostic standard was elevated cardiac isoenzyme levels, diagnostic changes on the ECG, or both. Study methods were reviewed to ensure that there were no duplications of patient samples included in our review. Of the 270 citations that were initially reviewed, 64 met the above criteria and were the basis for our results. The authors of one study (33) provided additional unpublished information that was included in our review.

Because some patients with acute coronary syndromes without infarction develop serious complications, we performed an additional analysis of bedside findings that are predictive of life-threatening arrhythmias, heart failure, or recurrent ischemic chest pain. Such bedside findings would help identify patients requiring more intensive monitoring, not just those with infarction.

Data Analysis

Any differences between the authors' 2 × 2 tables were settled by consensus. Sensitivity, specificity, and likelihood ratios were calculated using standard definitions (34). When a cell of a 2 × 2 table was 0, 0.5 was added to all cells before calculating likelihood ratios or estimating pooled estimates. Pooled estimates were calculated using the DerSimonian and Laird random-effects model (35), which considers both variance within the study and among studies. Data are presented using likelihood ratios because they can be easily applied in the clinical setting to estimate post-test probability of disease (36).

RESULTS

Coronary Artery Disease

The overwhelming majority of patients in these studies presented to outpatient clinics with stable, intermittent chest pain and were subsequently referred for coronary angiography. Most studies (14,17,19,22,33,37,38) excluded patients with known valvular heart disease or nonischemic cardiomyopathy. Some studies used >50% stenosis of any epicardial vessel as the diagnostic standard (13,14–17,19, 22–29,37–45), whereas others used >70% to 75% stenosis (18,20,21,33,46–48).

The most useful findings that argued for a diagnosis of coronary artery disease were the presence of typical angina (likelihood ratio [LR] = 5.8), serum cholesterol level >300 mg/dL (LR = 4.0), history of prior myocardial infarction (LR = 3.8), and age >70 years (LR = 2.6) (Table 2). In contrast, the most useful findings that argued against a diagnosis were nonanginal chest pain (LR = 0.1), pain duration >30 minutes (LR = 0.1), intermittent dysphagia (LR = 0.2), female sex (LR = 0.3), serum cholesterol level <200 mg/dL (LR = 0.3), and absence of classic risk factors for coronary artery disease (LR = 0.3).

The calculated likelihood ratios were pooled from studies that used two diagnostic criteria for coronary artery disease (>50% stenosis and >70% to 75% stenosis). When these diagnostic standards were analyzed separately, the pooled likelihood ratios remained the same. In studies using >50% stenosis as the diagnostic standard, the pooled likelihood ratios were 5.6 for typical angina, 1.1 for atypical angina, and 0.1 for nonanginal chest pain; in those using the diagnostic standard of >70% to 75% stenosis, the pooled likelihood ratios were 5.6 for typical angina, 1.3 for atypical angina, and 0.1 for nonanginal chest pain. The calculated likelihood ratios also included studies that combined patients with prior myocardial infarction with those without a history of myocardial infarction, but again the results were the same if only those studies excluding prior myocardial infarction were analyzed. In such studies, the pooled likelihood ratios were 5.8 for typical angina, 1.3 for atypical angina, and 0.1 for nonanginal chest pain.

Other than cholesterol values >300 mg/dL or <200 mg/dL, individual risk factors were found to contribute relatively little to the diagnosis of coronary artery disease. The pooled likelihood ratios for hypertension, diabetes, smoking, moderate hypercholesterolemia, family history of coronary artery disease, and obesity were each 2.3 or less, meaning that the presence of any of these risk factors shifted the probability of disease very little. Even combinations of risk factors increased the probability of disease by only a small amount.

Overall, the physical examination and ECG provided little additional diagnostic information. The presence of an ear lobe crease increased the probability of coronary artery disease minimally (LR = 2.3). Arcus senilis and an ankle-brachial index <0.9 lacked statistical significance, and the findings of chest wall tenderness, a normal ECG, and resting ST-T–wave abnormalities were diagnostically unhelpful.

Myocardial Infarction

Patients in these studies presented to emergency departments complaining of chest pain that was unrelated to trauma and unexplained by the chest radiograph. Most patients were hospitalized in telemetry or coronary care units for further monitoring and testing, although some investigators (7,30,49–52) followed all patients, including those discharged home from the emergency department.

The most discriminatory bedside finding in these patients was the ECG (Table 3). The most useful findings for diagnosing myocardial infarction were new ST elevation or ST elevation of unknown duration (LR = 22), Q waves (LR = 22), and ST depression (LR = 4.5). The following findings also increased the probability of infarction, although by much smaller amounts in comparison with electrocardiographic findings: systolic blood pressure <100 mm Hg (LR = 3.6), radiation of pain to the arm (right arm: LR = 4.7; left arm: LR = 1.8), an S_3 gallop (LR = 3.2), diaphoresis on examination (LR = 2.9), diastolic blood pressure <60 mm Hg (LR = 2.5), and presence of jugular venous distention (LR = 2.4).

Several bedside findings argued against the diagnosis of myocardial infarction, the most important of which was a normal ECG (LR = 0.2). Other findings arguing against infarction included age <40 years; pain that was pleuritic, sharp, or positional; and chest wall tenderness; with likelihood ratios ranging from 0.2 to 0.3.

Again, the presence or absence of traditional risk factors—male sex, hypertension, diabetes, tobacco use, elevated cholesterol level, or a family history of coronary artery disease—had little or no diagnostic value in diagnosing myocardial infarction (all likelihood ratios were

Table 2. Diagnosing Coronary Artery Disease in Patients with Stable, Intermittent Chest Pain

Finding (References)	No. of Patients	Sensitivity Range (%)	Specificity Range (%)	If Finding is: Present Likelihood Ratio* (95% Confidence Interval)	If Finding is: Absent Likelihood Ratio* (95% Confidence Interval)
Classification of chest pain					
Typical angina (13–20)	11,544	50–91	78–94	5.8 (4.2–7.8)	..
Atypical angina (13,14,16,19,20)	11,182	8–44	62–94	1.2 (1.1–1.3)	..
Nonanginal chest pain (13,14,16,19,20)	11,182	4–22	14–50	0.1 (0.1–0.2)	..
Other pain characteristics					
Burning pain (22)	250	4	94	0.6 (0.2–1.9)	1.0 (1.0–1.1)
Precipitating factors					
Emotional stress (21,22)	380	15–52	32–81	0.8 (0.6–1.0)	1.2 (0.9–1.6)
Food (21,22)	380	13–25	81–91	1.3 (0.3–4.9)	0.9 (0.7–1.2)
Lying flat (21,22)	380	14–22	82–89	1.2 (0.5–3.0)	1.0 (0.8–1.2)
Inspiration (22)	250	1	94	0.2 (0.0–1.0)	1.1 (1.0–1.1)
Alleviating factors					
Nitroglycerin (21,22)	380	60–74	29–56	1.2 (0.9–1.6)	0.7 (0.6–0.9)
Nitroglycerin within 5 minutes (21,22)	380	53–63	69–71	1.9 (1.4–2.4)	0.6 (0.5–0.8)
Associated symptoms					
Dizziness (22)	250	18	64	0.5 (0.3–0.8)	1.3 (1.1–1.5)
Dyspnea (22)	250	63	30	0.9 (0.8–1.1)	1.2 (0.8–1.8)
Heart burn (21)	130	38	63	1.0 (0.7–1.6)	1.0 (0.7–1.3)
Dysphagia (21)	130	5	80	0.2 (0.1–0.8)	1.2 (1.0–1.4)
Duration of chest pain (21)					
<5 minutes	130	86	65	2.4 (1.7–3.4)	0.2 (0.1–0.4)
>30 minutes	130	1	86	0.1 (0.0–0.9)	1.2 (1.0–1.3)
Frequency of chest pain (46)					
>1/day	100	50	69	1.6 (0.9–3.0)	..
<1/day and >1/wk	100	19	81	1.0 (0.4–2.5)	..
<1/wk	100	31	50	0.6 (0.4–1.0)	..
Radiation (22)					
Left arm	250	35	58	0.8 (0.6–1.2)	1.1 (0.9–1.4)
Right arm	250	21	86	1.5 (0.8–2.8)	0.9 (0.8–1.0)
Neck	250	19	80	1.0 (0.6–1.6)	1.0 (0.9–1.1)
Reproducibility score = 10 (21,22)	380	68–78	62–65	2.0 (1.6–2.4)	0.4 (0.3–0.6)
Angina scale (21,22)					
0 points	363	7–19	75–86	0.6 (0.1–2.9)	..
1 points	363	11–14	47–69	0.3 (0.2–0.6)	..
2 points	363	33–34	76–80	1.5 (1.0–2.1)	..
3 points	363	35–47	80–86	2.4 (1.6–3.5)	..
Risk factors					
Male sex (14,15,19,25,27,33,39,40,47)	17,593	72–88	36–58	1.6 (1.5–1.7)	0.3 (0.3–0.4)
Age (years)					
<30 (14,33)	14,569	0–1	97–98	0.1 (0–1.1)	..
30–49 (14,27,33,40,47)†	15,681	16–38	47–57	0.6 (0.5–0.7)	..
50–70 (14,33,40,47)	15,481	62–73	44–56	1.3 (1.3–1.4)	..
>70 (14,33,41,47)	15,266	2–52	67–99	2.6 (1.8–4.0)	..
Hypertension (22,27,39,42,47,48)	1478	36–60	55–78	1.2 (1.0–1.6)	0.9 (0.7–1.0)
Diabetes mellitus (22,27,39,42,47,48)	1478	10–29	86–97	2.3 (1.7–3.1)	0.9 (0.8–0.9)
Current/past tobacco use (22,27,39,42,47,48)	1478	42–77	47–68	1.5 (1.3–1.6)	0.7 (0.6–0.8)
Cholesterol (mg/dL) (37,38)					
<200	1585	10–11	58–71	0.3 (0.2–0.4)	..
201–250	1585	27–31	60–65	0.8 (0.7–0.9)	..
251–300	1585	34–35	76–83	1.7 (1.2–2.3)	..
>300	1585	24–29	93–94	4.0 (2.5–6.3)	..

(continued)

Table 2. Diagnosing Coronary Artery Disease in Patients with Stable, Intermittent Chest Pain—Continued

Finding (References)	No. of Patients	Sensitivity Range (%)	Specificity Range (%)	If Finding is: Present — Likelihood Ratio* (95% Confidence Interval)	If Finding is: Absent — Likelihood Ratio* (95% Confidence Interval)
Family history of coronary artery disease (22,42,47,48)	1003	41–65	33–57	1.0 (0.9–1.1)	1.0 (0.9–1.1)
Prior myocardial infarction (13,15,33,39,42,43,47)	8216	42–69	66–99	3.8 (2.1–6.8)	0.6 (2.1–0.6)
Obesity (27,48)	387	43–45	54–74	1.3 (0.8–2.1)	0.9 (0.7–1.1)
Number of risk factors (33)‡					
None	6434	7	78	0.3 (0.3–0.4)	—
Any 1	6434	35	57	0.8 (0.8–0.9)	—
Any 2	6434	39	73	1.4 (1.3–1.6)	—
3 or more	6434	18	92	2.2 (1.9–2.6)	—
Physical examination					
Earlobe crease (23–27)	1338	26–80	33–96	2.3 (1.3–4.1)	0.6 (0.4–0.8)
Chest wall tenderness (21,22,44)	442	1–25	69–97	0.7 (0.4–1.1)	1.0 (1.0–1.1)
Ankle-brachial index <0.9 (29)	165	20	95	4.1 (1.0–17)	0.8 (0.8–0.9)
Arcus senilis (28)	200	40	86	3.0 (1.0–8.6)	0.7 (0.6–0.8)
Electrocardiogram					
Normal (13,45)	309	23–33	50–69	0.7 (0.3–1.6)	1.2 (0.8–1.9)
ST-T-wave abnormalities (13,20,43)	2652	14–44	73–93	1.4 (1.0–1.9)	0.9 (0.9–1.0)

* Likelihood ratio if finding is present = positive; ratio if finding is absent = negative.

† Pooled estimate for age 30 to 49 years includes two studies (28,39) that combined age <30 years and age 30 to 49 years.

‡ Risk factors in this study included smoking (>25 pack-years or more than half pack per day within 5 years of catheterization), diabetes mellitus, hypertension (systolic >140 mm Hg), and hyperlipidemia (fasting cholesterol level >250 mg/dL).

close to 1.0). A prior history of myocardial infarction and associated dyspnea were also unhelpful diagnostically.

We had also sought to determine the diagnostic value of the response of chest pain to antacid medication (i.e., relief of pain with oral administration of 5 to 20 cc of viscous lidocaine solution plus 20 to 30 cc of magnesium-aluminum antacid), a diagnostic maneuver often used to differentiate between gastroesophageal and cardiac causes of acute chest pain. Because this test was assessed in only two studies (63,64) that also failed to use an accepted diagnostic standard for infarction, this analysis was not performed.

Life-Threatening Complications

Using a simple classification of patients in emergency departments based on the ECG and three additional findings from the patient interview and examination (Table 1), it was possible to stratify patients into risk categories predicting the development of life-threatening complications. Compared with low-risk patients, high-risk patients were almost nine times more likely to experience major complications during the first 24 hours (Table 4).

DISCUSSION

In 1768, Heberden described typical angina as a "most disagreeable sensation in the breast" that seizes patients "while they are walking" yet vanishes "the moment they stand still" (1). Modern definitions of typical angina (Table 1) retain Heberden's triad of essential ingredients—substernal discomfort, aggravation by exertion, and relief with rest—adding only that typical angina requires relief within 10 minutes of rest or within 10 minutes of taking nitroglycerin. Our review shows that this definition of typical angina remains the most compelling argument for the diagnosis of coronary artery disease in patients with stable, intermittent chest pain. Attempts to improve this definition by using more precise angina scoring schemes (Tables 1 and 2) or by isolating specific characteristics of the patient's chest pain are less accurate than this global assessment of Heberden's essential features.

Chest pain lacking Heberden's essential features—pain unrelated to activity, unrelieved by nitroglycerin, and otherwise not suggestive of angina (i.e., nonanginal chest pain)—was the most compelling argument against the diagnosis of coronary artery disease in our review. Although the term "otherwise not suggestive of angina" was not precisely defined in the studies reviewed, chest pain that was sharp, positional, or pleuritic argued against infarction, and presumably these atypical features, would argue against coronary artery disease among patients with stable, intermittent chest pain as well. Indeed, the point estimate for pleuritic pain in diagnosing

Table 3. Diagnosing Myocardial Infarction in Patients with Acute Chest Pain

Finding (References)	No. of Patients	Sensitivity Range (%)	Specificity Range (%)	If Finding is: Present Likelihood Ratio* (95% Confidence Interval)	If Finding is: Absent Likelihood Ratio* (95% Confidence Interval)
Quality of pain					
Oppressive or pressure-like (7,49,50,53–55)	11,504	51–82	31–65	1.3 (1.2–1.5)	0.7 (0.6–0.8)
Severe (51,55)	596	74–80	36–72	1.8 (0.9–3.8)	0.4 (0.3–0.7)
Sharp (7,50)	1088	8–16	59–70	0.3 (0.2–0.5)	1.3 (1.3–1.4)
Burning, indigestion (7)	596	10	93	1.4 (0.7–2.8)	1.0 (0.9–1.0)
Aching (7)	596	10	86	0.7 (0.4–1.3)	1.1 (1.0–1.1)
Worse than prior angina or similar to prior myocardial infarction (49)	7734	34	81	1.8 (1.6–2.0)	0.8 (0.8–0.9)
Positional (7,49)	8330	3–11	75–87	0.3 (0.2–0.5)	1.1 (1.1–1.2)
Pleuritic (7,49,50)	8822	3–6	74–82	0.2 (0.2–0.3)	1.2 (1.2–1.3)
Timing of pain (54)					
Duration >60 minutes	278	89	31	1.3 (1.2–1.5)	0.3 (0.2–0.6)
Sudden onset	278	70	34	1.1 (0.9–1.3)	0.9 (0.6–1.3)
Pain location					
Substernal (49,55)	7934	85–93	20–33	1.2 (1.1–1.3)	0.5 (0.4–0.5)
Radiation					
Jaw, neck, left arm or shoulder (49)	7734	48	66	1.4 (1.3–1.5)	0.8 (0.7–0.8)
Left arm (53,54)	2482	34–55	76	1.8 (1.1–2.8)	0.7 (0.5–1.1)
Right arm or shoulder (50,54)	770	15–41	94–95	4.7 (1.9–12)	0.8 (0.5–1.1)
Associated symptoms					
Nausea (50,51,53–55)	3665	24–56	70–84	1.7 (1.3–2.3)	0.8 (0.7–0.9)
Diaphoresis (49–51,53,55)	11,121	24–61	73–84	2.1 (1.8–2.5)	0.7 (0.6–0.8)
Dyspnea (51,53)	2695	36–49	52–66	1.0 (0.9–1.2)	1.0 (0.9–1.1)
Risk factors					
Male sex (7,49,51,53,54,56,57)	13,721	59–72	33–61	1.3 (1.2–1.4)	0.7 (0.7–0.7)
Age (years)					
<40 (7)	596	4	81	0.2 (0.1–0.5)	–
40–59 (7)	596	34	57	0.8 (0.6–1.1)	–
>60† (7,49,54)	8608	47–74	54–68	1.5 (1.4–1.6)	–
Hypertension (53,54,56,57)	4995	30–60	50–74	1.2 (1.1–1.3)	0.9 (0.8–1.0)
Diabetes mellitus (53,56–58)	7411	14–26	82–89	1.3 (1.1–1.6)	1.0 (0.9–1.0)
Tobacco use (51,57)	1870	32–38	65–76	1.3 (1.1–1.5)	0.9 (0.8–1.0)
Elevated cholesterol level (53)	2204	30	83	1.7 (1.3–2.3)	0.8 (0.8–0.9)
Family history of coronary artery disease (53)	2204	24	79	1.2 (0.8–1.6)	1.0 (0.9–1.1)
Prior myocardial infarction (7,49,50,53,56,57)	13,539	14–69	52–90	1.3 (1.0–1.8)	0.9 (0.8–1.0)
Angina (50,53,56,57)	5209	21–51	54–87	1.2 (0.9–1.8)	0.9 (0.8–1.1)
Heart failure (53,56,57)	4717	11–20	68–89	0.7 (0.6–0.9)	1.1 (1.0–1.2)
Obesity (54)	278	48	67	1.4 (1.1–1.9)	0.8 (0.6–1.0)
Physical examination					
Systolic blood pressure <100 mm Hg (57)	1592	6	98	3.6 (2.0–6.5)	1.0 (0.9–1.0)
Diastolic blood pressure <60 mm Hg (57)	1592	5	98	2.5 (1.3–4.8)	1.0 (0.9–1.0)
Diaphoresis (49,50)	8226	28–53	73–94	2.9 (1.3–6.6)	0.7 (0.6–0.8)
Jugular venous distention (53)	2204	10	96	2.4 (1.4–4.2)	0.9 (0.9–1.0)
Pulmonary crackles (50,53)	2696	20–38	82–91	2.1 (1.6–2.8)	0.8 (0.7–1.0)
S_3 gallop (50)	492	16	95	3.2 (1.6–6.5)	0.9 (0.8–1.0)
Chest wall tenderness (7,49,50)	8822	3–15	64–83	0.3 (0.2–0.4)	1.3 (1.1–1.4)
Reproducible with position change (7,49)	8330	3–11	75–87	0.3 (0.2–0.5)	1.1 (1.1–1.2)
Electrocardiogram‡					
Normal (7,52,54,57,59,60)	14,699	1–13	48–77	0.2 (0.1–0.3)	1.5 (1.4–1.6)
Nonspecific ST changes (7,60)	7711	5–7	47–78	0.2 (0.1–0.6)	1.5 (0.9–2.6)

(continued)

Table 3. Diagnosing Myocardial Infarction in Patients with Acute Chest Pain—Continued

Finding (References)	No. of Patients	Sensitivity Range (%)	Specificity Range (%)	If Finding is: Present Likelihood Ratio* (95% Confidence Interval)	If Finding is: Absent Likelihood Ratio* (95% Confidence Interval)
ST elevation (50,57,59–62)	15,287	31–49	97–100	22 (16–30)	0.6 (0.6–0.6)
ST depression (50,57,59,60)	13,848	20–62	88–96	4.5 (3.6–5.6)	0.8 (0.7–0.9)
Q wave (50,57,59)	6733	10–34	96–100	22 (7.6–62)	0.8 (0.8–0.9)
T-wave inversion (50,57,59)	6733	9–39	84–94	2.2 (1.8–2.6)	0.9 (0.8–1.0)
Conduction defect (50,57)	2084	13–14	86–98	2.4 (0.4–15)	1.0 (0.8–1.1)

* Likelihood ratio if finding is present = positive; ratio if finding absent = negative.
† Includes one study with age >65 years (49).
‡ All electrocardiographic abnormalities refer to findings that are new or of unknown duration.

coronary disease (LR = 0.2) equaled that for diagnosing infarction but lacked statistical significance. As expected, associated dysphagia also argued against the presence of coronary artery disease, but other symptoms traditionally associated with esophageal disease (e.g., heartburn and pain aggravated by lying flat) lacked diagnostic value because they were found just as frequently in patients with chest pain from coronary artery disease as in patients with chest pain from noncardiac causes. For the same reason, associated dyspnea, pain aggravated by emotional stress, and pain provoked by meals also lacked diagnostic value.

One surprising finding was that traditional risk factors (other than the extremes in cholesterol values and the absence of all risk factors) failed to greatly influence the probability of coronary artery disease or myocardial infarction among patients presenting with chest pain. Even the presence of multiple risk factors failed to increase the probability of coronary artery disease greatly among patients referred for catheterization. One possible explanation is that there are important interactions between risk factors and other patient variables not identified by our review; for example, it is possible that hyperlipidemia has greater diagnostic accuracy in younger than older patients. Although we could not test this hypothesis for most risk factors, we were able to test it for diabetes and found no such interaction; the likelihood ratio for diabetes in diagnosing coronary disease was similar for patients younger than 50 years (LR = 2.4) as it was for the entire study population (LR = 2.3). Instead, the most likely explanation why risk factors of proven etiologic importance in longitudinal studies lack diagnostic utility is that their association with coronary artery disease is relatively weak (compared with the diagnostic value of typical angina, for example) (65,66) or that the same risk factors are linked to illnesses causing noncardiac chest pain (67), thus limiting their discriminatory value.

Physical examination, once the foundation of cardiovascular diagnosis in the era of rheumatic heart disease, has much less diagnostic value in the era of coronary artery disease. One thoroughly investigated finding, the earlobe crease, does increase the probability of coronary artery disease, but by only a small amount of doubtful clinical utility. Although the earlobe crease has been suspected to be nothing more than a surrogate for other cardiovascular risk factors (68), most studies show that the finding is independent of age (24,25,27,69,70) and cholesterol level (26). Two other findings, arcus senilis and an ankle-brachial in-

Table 4. Predicting Life-Threatening Complications* in Patients with Acute Chest Pain

Risk Category† (References)	No. of Patients	Sensitivity Range (%)	Specificity Range (%)	Likelihood Ratio If Finding Is Present (95% Confidence Interval)
High (30–31)	30,683	51–88	92–93	8.7 (4.4–17)
Moderate/low (30–31)	30,683	13–42	59–66	1.2 (0.6–2.1)
Very low‡ (30–32)	31,360	7–13	42–53	0.1 (0.1–0.2)

* Life-threatening complications (in first 24 hours of hospitalization) include arrhythmias (ventricular fibrillation, cardiac arrest, new complete heart block, insertion of temporary pacemaker, emergency cardioversion), pump failure (cardiogenic shock, use of intraaortic balloon pump, intubation), and ischemia (recurrent ischemic chest pain requiring bypass surgery or percutaneous intervention).
† Defined in Table 1.
‡ One study (32) used a systolic blood pressure cutoff of ≤100 mm Hg as a risk factor, instead of a cutoff of ≤110 mm Hg.

dex <0.9, show promise as diagnostic signs but require further study.

We found the ECG to be the most important bedside finding in diagnosing myocardial infarction and predicting early complications in patients with acute chest pain, which contrasts with its lack of value in diagnosing coronary artery disease among patients with stable chest pain. Since the ECG is also one of the diagnostic criteria for infarction in studies of acute chest pain, this conclusion initially seems to be circular. Nonetheless, it is important to recognize that only pathologic Q waves were used as the electrocardiographic diagnostic standard in these studies, and that this finding had a sensitivity of only 10% to 34%, indicating that most, if not all, patients with infarction were diagnosed using cardiac isoenzyme measurements. The most compelling electrocardiographic finding, ST elevation, as well as the other electrocardiographic findings reviewed in Table 3, were not diagnostic standards in these studies.

There were two additional contrasts between the diagnoses of coronary disease and myocardial infarction. Prior history of myocardial infarction increased the probability of coronary disease in patients with stable, intermittent chest pain but failed to increase the probability of infarction in patients with acute chest pain. This probably occurs because patients with prior infarction are concerned about any recurrent chest pain and present to emergency departments frequently with noncardiac chest pain or with angina but no infarction. Another contrast was that the finding of chest wall tenderness argued against infarction in patients with acute chest pain, yet the same finding lacked diagnostic value in patients with stable, intermittent chest pain. This observation possibly reflects the high prevalence of disorders in the chest wall among patients without infarction in studies of acute chest pain.

Although no study of the use of antacid medications met our selection criteria, studies do show that antacid medications may paradoxically relieve the pain of myocardial infarction in some patients (63,71), as well as the pain due to other nondyspeptic disorders such as cholecystitis and pancreatitis (72). These studies also show that interpretation of this test is difficult because the antacid is often administered soon before or after the administration of other active drugs (e.g., narcotics, nitroglycerin, histamine antagonists) (64).

By using the ECG, patient history, and physical examination, clinicians can stratify patients with acute chest pain into groups indicating high or very low risk of developing life-threatening complications. Other investigators have previously shown that this risk stratification method is more accurate than physicians' usual triage decisions (73) and that this rule identifies up to one third of patients admitted with suspected acute ischemic chest pain that could be managed safely with less intensive care (31).

We conclude that the most important finding when diagnosing coronary artery disease is the description of the patient's pain, and the most important finding when diagnosing infarction or predicting life-threatening complications is the ECG. A few physical findings have modest diagnostic value, but other than the extremes in cholesterol values, the analysis of risk factors changes the probability of coronary artery disease or infarction very little or not at all.

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