

Diagnostic performance of serial serum total tryptase measurement to differentiate positive from negative allergy testing among patients with suspected perioperative hypersensitivity

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Abstract

Background

Serum total tryptase has been shown to increase during acute allergic reactions (acute tryptase, T_A); however, few studies have investigated the values of T_A or a combination of T_A and baseline tryptase (T_B) to discriminate positive from negative testing in perioperative hypersensitivity reaction (POH) allergy work up. The aim of this study was to determine the diagnostic performance of T_A in order to differentiate positive from negative allergy testing suspected POH and analyze the diagnostic performance of serial tryptase levels using several formulas.

Methods

All patients from the University hospital of Montpellier and Strasbourg, France who presented with suspected POH and underwent complete drug allergy work-up between March 2011 and December 2019 with available T_A and T_B were included. Four formulas, including a change in $T_A > 11$ (F1), or $> 2 + 1.2 \times T_B$ (F2), or $> 3 + T_B$ (F3), or $> 120\% T_B$ (F4), were applied.

Results

One hundred and sixty-two patients were included, and 131 of them (80.8%) had grade III or IV reactions. Ninety patients had positive allergy testing. The optimal cut-off value of T_A to distinguish positive from negative allergy testing patients was 9.8 $\mu\text{g/L}$ with an AUC of 0.817 (95%CI: 0.752-0.882, $p < 0.001$). The 93% PPV threshold for T_A was 33 $\mu\text{g/L}$ (95.8%

specificity). Paired tryptase levels according to formulas F2 and F3 yielded the highest Youden index (0.54 and 0.53, respectively).

Conclusion

The optimal cut-off point for T_A for distinguishing positive from negative allergy testing suspected POH was 9.8 $\mu\text{g/L}$. T_A value of 33 $\mu\text{g/L}$ was required to achieve >90% PPV.

Supporting Information



Filename	Description
cea14040-sup-0001-FigS1-S3.docx Word document, 59.1 KB	Fig S1-S3
cea14040-sup-0002-TableS1-S3.docx Word document, 24 KB	Table S1-S3

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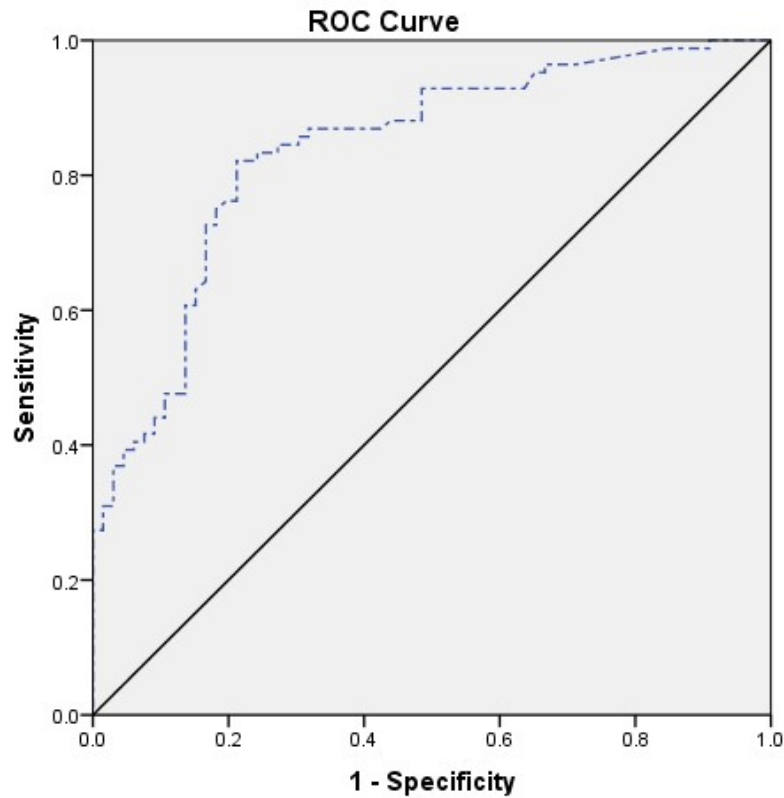
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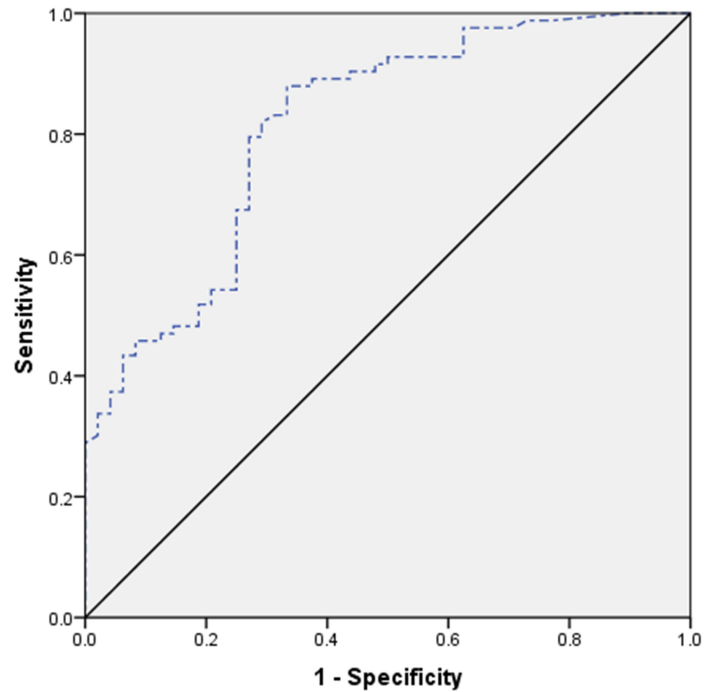
Figure E1. Receiver operating characteristic (ROC) curve analysis to determine the optimal cutoff value of T_A for differentiating between the positive and negative allergy work-up groups among patients without elevated T_B (n=150)



Cut-off value T_A	Sensitivity	Specificity	PPV	NPV
2.32	100	9.1	58.3	100
3.69	95.2	34.8	65.0	85.2
9.8	82.1	78.8	83.1	77.6
16.9	60.7	86.4	85.0	63.3
29.8	39.3	95.5	91.7	55.3
43.5	31.0	97.0	92.9	52.5
49.4	31.0	98.5	96.3	52.8
54.5	27.4	100	100	52.0

Abbreviations: NPV, negative predictive value; PPV, positive predictive value

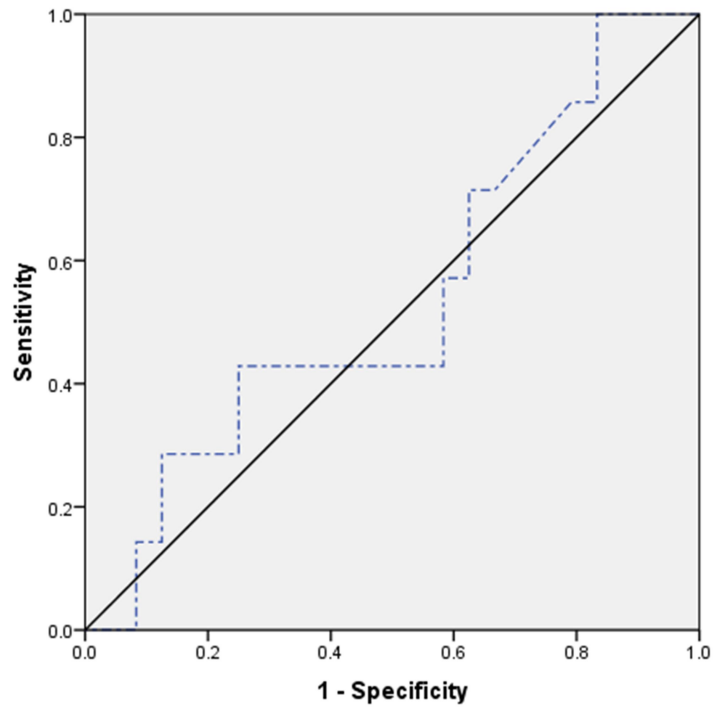
Figure E2. Receiver operating characteristic (ROC) curve analysis to determine the optimal cutoff value of T_A for differentiating between the positive and negative allergy work-up groups among patients with grade III or IV reactions (n=131)



Cut-off value T_A	Sensitivity	Specificity	PPV	NPV
2.85	100	10.4	65.9	100
4.82	95.2	37.5	72.5	81.8
9.80	88.0	66.7	82.0	76.2
23.85	51.8	81.2	82.7	49.4
45.40	37.3	95.8	93.9	46.9
54.50	33.7	97.9	96.6	46.2
60.45	28.9	100	100	44.9
2.85	100	10.4	65.9	100

Abbreviations: NPV, negative predictive value; PPV, positive predictive value

Figure E3. Receiver operating characteristic (ROC) curve analysis to determine the optimal cutoff value of T_A for differentiating between the positive and negative allergy work-up groups among patients with grade I or II reactions (n=31)



Cut-off value T_A	Sensitivity	Specificity	PPV	NPV
2.32	100	16.7	25.9	100
2.89	71.4	25.0	21.7	75.0
9.80	28.6	87.5	40.0	80.8

Abbreviations: *NPV*, negative predictive value; *PPV*, positive predictive value

Table E1. Demographic data, clinical history of perioperative hypersensitivity reaction, and identified culprit allergens compared between the two centers

Characteristics	Montpellier (n=88)	Strasbourg (n=74)	<i>P</i>
Male gender	39 (44.3)	23 (31.1)	0.06
Median age at the time of reaction (years; IQR) [†]	56.5 (43-65.8)	56 (46-65)	0.78
Severity grading scale			0.05
I	6 (6.8)	14 (18.9)	0.02
II	4 (4.6)	7 (9.4)	0.22
III	70 (79.5)	48 (64.9)	0.04
IV	8 (9.1)	5 (6.8)	0.59
Symptoms			
Cutaneous	38 (43.2)	31 (41.9)	0.50
Respiratory	34 (38.6)	24 (32.4)	0.26
Cardiovascular	81 (92.1)	56 (75.7)	0.004
Result of allergy work-up			0.008
Allergic group	57 (64.8)	33 (44.6)	
Non-allergic group	31 (35.2)	41 (55.4)	
Allergens identified [‡]			0.04
Neuromuscular blocking agents	30 (50.8)	21 (61.8)	0.46
Antibiotics	17 (28.8)	9 (26.4)	0.23
Chlorhexidine	5 (8.5)	-	0.04
Others	7 (11.9)	4 (11.8)	0.53
Median level of T _B (μg/L; IQR)	4.5 (3.2-6.6)	3.0 (2.7-4.9)	<0.001
Median level of T _A (μg/L; IQR)	18.8 (7.7-51.3)	8.42 (3.4-20.9)	<0.001

[†]5 missing data (n=69 in Strasbourg)

[‡] 90 patients with 93 confirmed allergens (two patients in Montpellier and one patient in Strasbourg had two identified allergens)

Abbreviations: *IQR*, interquartile range; *T_A*, acute serum total tryptase; *T_B*, baseline serum total tryptase

Bolded values are considered statistically significant (*p*<0.05)

Table E2. Diagnostic performance of T_A for distinguishing positive from negative allergy work-up patients among cases with $T_B \leq 11 \mu\text{g/L}$

Table E2.1. All patients with $T_B \leq 11 \mu\text{g/L}$ (n=150)

	$T_A > 11 \mu\text{g/L}$ (F1)	$T_A > 2\mu\text{g/L} + (1.2 \times T_B)$ (F2)	$T_A > (3 \mu\text{g/L} + T_B)$ (F3)	$T_A > 120\% T_B$ (F4)
Sensitivity (%)	76.2	88.1	88.1	94.0
Specificity (%)	78.8	66.7	65.2	47.0
PPV (%)	82.1	77.1	76.3	69.3
NPV (%)	72.2	81.5	81.1	86.1
Positive LR	3.59	2.65	2.53	1.77
Negative LR	0.30	0.18	0.18	0.13
Youden index	0.55	0.55	0.53	0.41

Table E2.2. Patients with grade III or grade IV reactions and $T_B \leq 11 \mu\text{g/L}$ (n=120)

	$T_A > 11 \mu\text{g/L}$ (F1)	$T_A > 2\mu\text{g/L} + (1.2 \times T_B)$ (F2)	$T_A > (3 \mu\text{g/L} + T_B)$ (F3)	$T_A > 120\% T_B$ (F4)
Sensitivity (%)	81.8	93.5	93.5	97.4
Specificity (%)	72.1	58.1	55.8	41.9
PPV (%)	84.0	80.0	79.1	75.0
NPV (%)	68.9	83.3	82.8	90.0
Positive LR	2.93	2.23	2.12	1.68
Negative LR	0.25	0.11	0.12	0.06
Youden index	0.54	0.52	0.49	0.39

Table E2.3. Patients with grade I or grade II reactions and $T_B \leq 11 \mu\text{g/L}$ (n=30)

	$T_A > 11 \mu\text{g/L}$ (F1)	$T_A > 2\mu\text{g/L} + (1.2 \times T_B)$ (F2)	$T_A > (3 \mu\text{g/L} + T_B)$ (F3)	$T_A > 120\% T_B$ (F4)
Sensitivity (%)	14.3	28.6	28.6	57.1
Specificity (%)	91.3	82.6	82.6	56.5
PPV (%)	33.3	33.3	33.3	28.6
NPV (%)	77.8	79.2	79.2	81.2
Positive LR	1.64	1.64	1.64	1.31
Negative LR	0.94	0.86	0.86	0.76
Youden index	0.06	0.11	0.11	0.14

Table E3. Characteristics of patients with $T_B > 11 \mu\text{g/L}$

Patient no.	Sex	Age at suspected POH (Yr)	T_B ($\mu\text{g/L}$)	T_A ($\mu\text{g/L}$)	Severity grading scale	Group (identified culprit)	Symptoms and signs during suspected POH		
							CU	CV	RS
1	F	61	24	86.3	III	Allergic (NMBA)	-	Yes	-
2	F	87	17.4	95.2	III	Allergic (ATB)	Yes	Yes	Yes
3	F	78	16	154	III	Allergic (NMBA)	-	Yes	Yes
4	F	43	14	141	III	Allergic (NMBA)	-	Yes	-
5	M	61	13	200	IV	Allergic (NMBA)	-	Yes	-
6	M	33	12.7	18.4	IV	Allergic (ATB)	Yes	Yes	Yes
7	M	67	22.7	26.2	IV	Non-allergic	-	Yes	-
8	F	42	27.3	28.2	III	Non-allergic	-	-	Yes
9	F	65	16.7	23.6	III	Non-allergic	Yes	Yes	-
10	M	75	16	60	III	Non-allergic	-	Yes	-
11	F	50	15.3	9.2*	III	Non-allergic	-	Yes	-
12	M	40	14	28.6	II	Non-allergic	-	Yes	Yes

Abbreviations: ATB, antibiotic; CU, cutaneous; CV, cardiovascular; Neuro-muscular blocking agents; POH, perioperative hypersensitivity reaction; RS, respiratory

* T_A was measured 20 minutes after the occurrence of the reaction