3.3 A PE Diagnosis

A pulmonary embolism (PE) is a blood clot in the lungs. There are many risk factors, including age >65 years, recent surgery, cancer, and a previous deep vein thrombosis (blood clot in a deep vein, DVT) or PE. It is an important consideration in the differential diagnosis of acute chest pain or shortness of breath because it is treatable (with anticoagulants) and can cause death if the diagnosis is missed. The "gold standard" (more or less) to make the diagnosis is a CT Pulmonary Angiogram (CTPA), but this entails cost and radiation, so we would prefer not to do it if the probability PE is low enough. For this problem, we will say we should **do a CTPA if the (posttest) probability of PE is ≥ 5%,** i.e., we are willing to do up to 20 CTPAs to diagnose one PE. *D-Dimer* is a clot degradation product present in blood when there is a blood clot. It is used clinically to help estimate the likelihood of a PE.

Duriseti and Brandeau[1] published a detailed evaluation of different strategies for diagnosing pulmonary embolism (PE). They estimated that among patients at risk of PE, the sensitivity of D-Dimer level ≥ 500 µg/L was 98.1% and the specificity was 45.8%.

a. What would be the LR+ for a D-Dimer level ≥ 500 µg/L?

   The LR+ would be sensitivity/(1−specificity) = 98.1%/(1-45.8%) = 1.8

b. Julie is 67 years old and has acute chest pain and shortness of breath, but no other PE risk factors or signs except her age. Her prior probability of PE is about 10%.[2] Her D-Dimer level is 575 µg/L. Based on the LR calculated in part A, should she get a CTPA?

   No calculations necessary. The LR is > 1, so this result will increase her pre-test probability, which is already above the threshold.

   Based on the LR calculated in part a, she should get a CTPA.

c. The D-Dimer test is not naturally dichotomous, so the cutoff chosen to define a positive test will determine the sensitivity and specificity, as shown in the (corrected) table from Duriseti and Brandeau below:

D-dimer Level: lower limit for abnl	Sensitivity for PE, %	Specificity for PE, %
Cutoff I (≥200 µg/L)	99.9	8.31
Cutoff II (≥350 µg/L)	99.8	30.0
Cutoff III (≥500 µg/L)	**98.1**	**45.8**
Cutoff IV (≥650 µg/L)	92.1	63.1
Cutoff V (≥800 µg/L)	80.0	76.1

Use the table above to estimate what percent of patients *with* a PE will have a D-Dimer level between 500 and 649 µg/L, as Julie does.

98.1% - 92.1% = 6%

d. Now estimate what percent of subjects *without* a PE will have a D-Dimer level in that range?

You could simply calculate this as 63.1% - 45.8% = 17.3%.

You could also use Excel to covert the table into a standard ROC table sorting results from most to least abnormal and reporting 1 –specificity instead of specificity. Then calculate the differences to create an LR table and calculate LRs:

	Sensitivity %	**1 - Specificity %**	**D+**	**D-**	
100000	0	0	**Interval %**	**Interval %**	**LR**
Cutoff V (≥800 µg/L)	80	23.9	80	23.9	3.35
Cutoff IV (≥650 µg/L)	92.1	36.9	12.1	13	0.93
Cutoff III (≥500 µg/L)	98.1	54.2	6	17.3	0.35
Cutoff II (≥350 µg/L)	99.8	70	1.7	15.8	0.11
Cutoff I (≥200 µg/L)	99.9	91.69	0.1	21.69	0.00
≥0	100	100	0.1	8.31	0.01

e. Use the general definition of a LR to calculate the LR for having a D-Dimer level between 500 and 649 µg/L.

6%/17.3% = 0.35

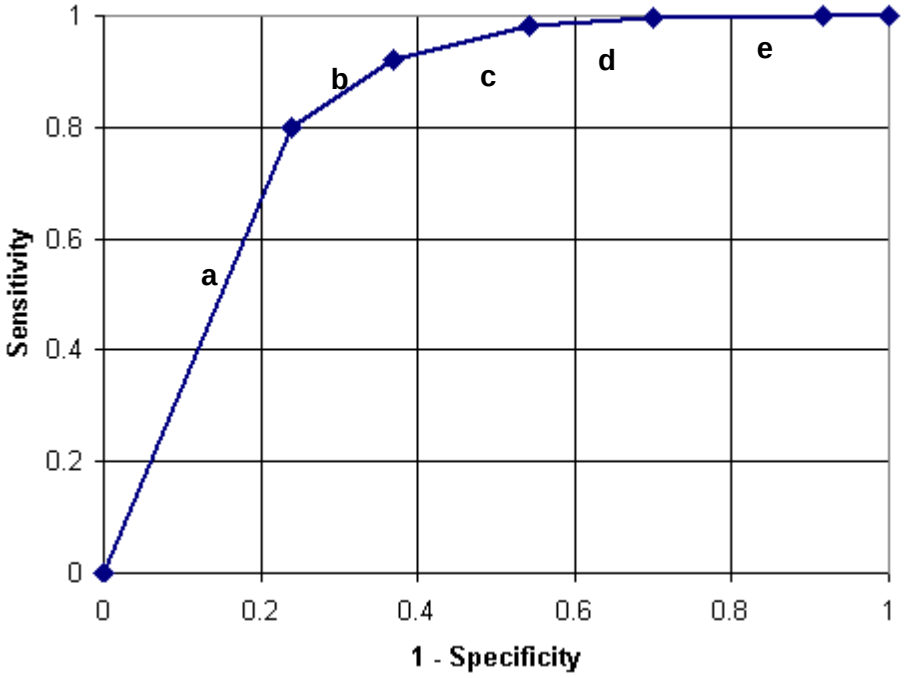
f. Use the LR from part e to estimate the posterior probability that Julie has a PE, given her prior probability of 10% and her D-Dimer of 575 µg/L.

Since her prior probability is 1/10, her prior odds are 1:9. Multiplying by the LR gives post-test odds of 0.35:9 and post-test probability of 0.35/9.35 = 3.7%

g. Recall that the threshold for ordering a CTPA was a 5% probability of PE. Should she get a CTPA? Discuss how the answers to parts b and f differ. Which estimate should you use?

Now she shouldn't get the CTPA, because her estimated probability of PE is below our CTPA testing threshold. Dichotomizing at ≥500 lumped all values ≥ 500 together into the LR(+), including values ≥ 800. But Julie only had a result of 575, which is very different from a result ≥ 800. This illustrates why it is important to use the interval LR. Dichotomizing non dichotomous tests will usually give the wrong answer, and this can lead to worse decisions and outcomes. It's why we are passionate about teaching this stuff!

h. The following ROC curve is based on the data in the table in part c above.



h.1 Which interval (provide the letter) on the curve corresponds to the D-Dimer interval between 500 and 650 µg/L? [1]

Answer: It must be the line segment corresponding to the 3rd most abnormal result. Since the most abnormal results are at the origin, it would be letter c.

h.2 Which D-Dimer levels corresponds to the letter **a**? [1]

***Answer: This is the segment corresponding to the most abnormal result, or ≥ 800* µg/L.**

REFERENCES

1. Duriseti RS, Brandeau ML. Cost-effectiveness of strategies for diagnosing pulmonary embolism among emergency department patients presenting with undifferentiated symptoms. Ann Emerg Med. 2010;56(4):321-32 e10.
2. Le Gal G, Righini M, Roy PM, Sanchez O, Aujesky D, Bounameaux H, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. Ann Intern Med. 2006;144(3):165-71.