Deacon's Challenge

No 194 - Answer

A GP asks your help interpreting plasma creatinine results obtained on a 56 year old hypertensive patient. At diagnosis his plasma creatinine was 85 µmol/L. Six months later his plasma creatinine had risen to 110 µmol/L. Although the eGFR on both specimens was reported as >60 mL/min/1.73m^2 he is concerned that the patient may be developing renal disease. Is this increase significant? Your laboratory quotes a reference range (95% confidence limits for a Gaussian distribution) of 60-120 µmol/L with an analytical CV of 6.3% at all concentrations above 80 µmol/L. Assume an index of individuality of 0.46.

Table of z-distribution:

P (two sided)	*0.10*	*0.05*	*0.02*	*0.01*	*0.002*	*0.001*
z	*1.65*	*1.96*	*2.33*	*2.58*	*3.09*	*3.29*

The first task is to calculate the combined analytical and intra-individual *CV*.

The reference range covers a 4*SD* range (mean±2*SD*). Therefore *SD* = (120 - 60)/4 = 15 µmol/L. At a mean of 90 µmol/L this corresponds to a *CV* of 15 x 100/90 = 16.7%.

$$CV_{Total}^2 = CV_{Biological}^2 + CV_{Analytical}^2$$

Substituting CV_{Total} = 16.7%, $CV_{Analytical}$ = 6.3% and solving for $CV_{Biological}$:

$$16.7^2 = CV_{Biological}^2 + 6.3^2$$

$$CV_{Biological} = \sqrt{(16.7^2 - 6.3^2)} = \sqrt{(278.9 - 39.7)} = \sqrt{239.2} = 15.5\%$$

This is the total biological variation and will be composed of the intra-individual *CV* (CV_{Intra}) and inter-individual *CV* (CV_{Inter}):

$$\text{Total } CV_{Biological}^2 = CV_{Intra}^2 + CV_{Inter}^2$$

The CV_{Intra} and CV_{Inter} are related by the index of individuality (in this case 0.46):

$$\text{Index of individuality} = CV_{Intra} = \frac{0.46}{CV_{Inter}}$$

Therefore substitute $CV_{Inter} = CV_{Intra}/0.46$ and total $CV_{Biological}$ = 15.5% and solve for CV_{Intra}:

$$15.5^2 = CV_{Intra}^2 + (CV_{Intra}/0.46)^2 = CV_{Intra}^2 + CV_{Intra}^2/0.212$$

$$15.5^2 \times 0.212 = 0.212CV_{Intra}^2 + CV_{Intra}^2$$

$$50.9 = 1.212CV_{Intra}^2$$

$$CV_{Intra} = \sqrt{(50.9/1.212)} = \sqrt{42.0} = 6.5\%$$

Next use the CV_{Intra} and $CV_{Analytical}$ to calculate the total *CV* for an individual's result:

$$\text{Individual's } CV_{Total} = \sqrt{(CV_{Analytical}^2 + CV_{Intra}^2)}$$
$$= \sqrt{(6.3^2 + 6.5^2)} = \sqrt{(39.7 + 42.3)} = \sqrt{82} = 9.1\%$$

In order to compare the two creatinine values (C_1 and C_2) calculate the *z*-score:

$$z = \frac{\text{Change in creatinine}}{\text{SD of the change}} = \frac{C_2 - C_1}{\text{SD of } (C_2 - C_1)}$$

SD of C_2 (110 µmol/L) = 110 x 9.1/100 = 10 µmol/L, *SD* of C1 (85 µmol/L) = 85 x 9.1/100 = 7.7 mmol/L

SD of $(C_2 - C_1) = \sqrt{(10^2 + 7.7^2)} = \sqrt{(100 + 59.3)} = \sqrt{159.3} = 12.6$ µmol/L

Substitute this *SD* of the difference to calculate *z*:

$$z = \frac{110 - 85}{12.6} = \frac{25}{12.6} = 2.0$$

Since we are only interested in detecting an increase in creatinine a value for z above 1.65 will only be obtained on 5% of occasions if no real increase has occurred, 2.0 is in excess of this supporting the hypothesis that the increase in plasma creatinine is statistically significant. If the index of individuality is ignored (so that a population *SD* of 15 µmol/L is used) then the *z*-score becomes 1.2 which is insignificant. The increase in creatinine is significant even though the value remains well inside the reference range and both eGFR results are greater than 60 mL/min/1.73m^2.

Question 195

A male anuric patient with a body weight of 84 Kg undergoes haemodialysis for 3 h. His plasma urea concentration was initially 20.5 mmol/L and after dialysis 5.4 mmol/L. Estimate the dialyser urea clearance in mL/min stating any assumptions that you make.