The F-Cell Ratio: A Clinically Important Parameter or Just Fine Tuning?

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Determination of the venous haematocrit is one of the simplest and oldest tests in laboratory medicine. However, its interpretation from a physiological and pathophysiological point of view remains controversial and is frequently associated with dogma and confusion. For most of this century it has been repeatedly questioned as to what is the true relationship between the haematocrit of blood obtained from the macro-circulation and that of the circulation as a whole [1,2]. What variation is there in haematocrit between the macro- and microcirculation and between different organs of the body, and do these relationships change with alterations in blood volume, red cell mass or plasma volume, and is the relationship altered by disease states? It is now generally accepted that the haematocrit of blood in macrocirculation is different from that obtained when the red cell mass and plasma volume are measured independently (body haematocrit). In the stable state in a normal person the relationship of the body haematocrit to the venous haematocrit is approximately 0.9, this is termed the F-cell ratio. This means that the venous haematocrit is 10% higher than that of the body haematocrit. The reasons for this have been debated over the years, and initially it was thought to be related to problems in accurately measuring red cell mass and/or plasma volume. In particular, methods used for measuring the plasma volume may have led to an overestimation due to leaking of the marker into the interstitium. This appears to be a relatively minor problem if plasma volume measurement techniques are carried out with due attention to detail. It is now accepted that the F-cell ratio represents variations in the red cell mass distribution within the vascular space. The haematocrit in the microcirculation is lower than that in the macrocirculation. In essence this means that the red cell mass circulates faster than the plasma. The hae-modilution in small vessels was first postulated by Fahraeus and is now generally accepted. The individual organs of the body autoregulate their own microcirculatory flow and haematocrit by the process of vasomotion. The F-cell ratio has been shown to vary under different circumstances. Can the F-cell ratio of 0.9 be used as a constant when calculating the total blood volume by measuring only one of its components (i. e. red cell mass or plasma volume) or should both parameters be measured to ensure and accurate result?

There has been controversy over the years as to whether the ratio is affected by anaemia or polycythaemia. Chaplin et al. originally demonstrated that there was consistency in the F-cell ratio over a wide haematocrit range [3]. As a result of these studies a standard correction factor has been used (usually F-cell ration of 0.9) when estimating red cell mass from plasma volume or vice versa. However, in recent years these findings have been disputed, and there is now agreement that there is a relationship between the haematocrit and the F-cell ratio and in the

presence of anaemia the F-cell ratio increases, indicating that there is less difference between the body haematocrit and the venous haematocrit [4, 5]. The presence of splenomegaly markedly reduces the F-cell ratio. This is predominantly due to the pooling of red cells in high intra-splenic haematocrit.

In this issue of the journal *INFUSIONSTHERAPIE* and *TRANSFUSIONSMEDIZIN* Haller et al. [6] address the question of whether haemodilution alters the F-cell ratio. This may be an important question, as the volume of red cells removed is commonly determined by monitoring the venous haematocrit. If the F-cell ratio alters during normovolemic haemodilution, changes in the haematocrit may not reflect true changes in the red cell mass.

In this study it was found that the red cell volumes calculated from measured plasma and venous haematocrit revealed a deficit in red cells after haemodilution when compared to the actual measured red cell volumes removed. The authors conclude that the only explanation for this could be an alteration in the F-cell ratio during the normovolemic haemodilution. This would have been a more elegant study if red cell mass had also been measured. This would have been relatively easy, especially using one of the newer red cell labelling techniques. If this had been included in the study, the authors' theory that the F-cell ratio changes during haemodilution could have been proven.

In this study Haller et al. accurately determine the volume of red cells removed and compare it with the usual clinical measures for estimating red cell loss on the basis of a falling

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haemoglobin level. This study may not only be relevant to intentional haemodilution, but may also be important in the setting of a haemorrhaging patient in elective surgery where replacement is on a normovolaemic basis [7, 8]. One could not extrapolate these studies to haemorrhage and haemodilution in the context of blood loss with associated hypovolaemia and/or shock. Methods are available for measuring most aspects of oxygen transport. However, blood volume, especially in a dynamic and changing situation, presents significant problems. The importance of knowing the circulatory blood, plasma and red cell volumes in unstable critically ill patients is unquestioned, and although methods have been available for measuring red cell mass and plasma volume for decades, their use is frequently cumbersome, not without interpretation problems and difficult to apply repeatedly in a dynamic and changing clinical situation.

If the haematocrit could be reliably used in conjunction with other important clinical indicators of oxygen transport in interpreting the status of the blood volume, haemodilution in general would be easier and safer. From their findings Haller et al. suggest that if the clinician is aware of the changing F-cell ratio in a patient during haemodilution, the haematocrit can still be a useful indicator of the progress of the haemodilution in terms of the number of red cells removed, as long as the rising F-cell ratio is taken into account as the haemoglobin concentration falls.

Circulating blood volume is thus clearly an important clinical parameter, relevant in the management of a wide range of patients. Whether one needs to always measure red cell mass and plasma volume concurrently for accurate determination of blood volume or whether it can be calculated from the venous haematocrit using the F-cell ratio as a correction factor remains sub judice and is not answered by Haller et al. Plasma volume is the component of the circulating blood volume which is most changeable in various physiological and clinical settings, as fluid may shift to or from the interstitial compartment, clear fluid may be lost from the body (e. g.

urine, sweat, gut) and alterations in venous capacitance or vasomotion require a homeostatic response by changing plasma volume to maintain the central blood volume and cardiac function [9]. In contrast circulating red cell mass only acutely changes if there is haemorrhage, haemolysis or transfusion. For this reason the most practical clinical measurements would be plasma volume estimations with use of the venous haematocrit to calculate the red cell mass and blood volume. In this context the use of the F-cell ratio and the knowledge of its variability in relation to the other parameters outlined above, may be clinically important as a correction factor.

Despite this optimism about the F-cell ratio it will always be difficult to establish standardized values for blood, plasma or red cell volumes, as these parameters relate to other patient variables, such as body weight, body surface area, sex, age, aerobic fitness and other life style factors. To complicate things even further, the absolute measured intravascular volume does not necessarily tell us all we need to know about the effective circulating volume and effective microvascular perfusion and function. The blood volume must always be assessed in relation to the size of the vascular compartment which fluctuates by changes in venous capacitance and microcirculatory vasomotion, with the ultimate aim of ensuring adequate cardiac filling pressures and cardiac output [9]. Every medical student knows that a human can lose as much as 80% of total red cell mass and survive if normovolaemia is maintained, by ensuring adequate plasma volume replacement. In contrast, loss of little more than a third of total blood volume without volume replacement is likely to be fatal.

To conclude, the practical role of the F-cell ratio in the overall clinical management of oxygen transport in a haemorrhaging patient or during haemodilution is in reality a very small fish in a very big pond. Venous haematocrit, in conjunction with many other 'numbers' will always remain one of the most important and simplest laboratory parameters in the assessment and management of oxygen transport. However, the astute physician will always apply well-tested clinical skills in conjunction with measurable parameters and intelligent estimation of other variables whether they can be measured or not. The F-cell ratio may be in the later category and may be more for 'fine tuning' decision making in assessing oxygen transport.

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70

Isbister

Clinical Usefulness of the F-Cell Ratio