



Laboratory measurement of Serum Free Light Chains (SFLC)

Insight – April 2015

- Serum free light chains (SFLC) can replace 24 hour urine electrophoresis and immunofixation in screening for monoclonal gammopathies.
- An abnormal SFLC ratio has prognostic significance in MGUS and myeloma.
- SFLC allows monitoring of patients with non-secretory myeloma.

Introduction

Immunoglobulins contain two heavy chains and two identical light chains, either kappa (κ) or lambda (λ). Each B cell clone secreting immunoglobulins produces either κ or λ light chains. The normal ratio of total κ/λ production is 0.3 – 1.7¹. Abnormalities in the amount or ratios of κ and λ light chains can be seen in benign disease states such as polyclonal hypergammaglobulinaemia and renal failure, in malignant plasma cell neoplasms such as multiple myeloma, AL amyloidosis, monoclonal gammopathy (MGUS), solitary plasmacytoma and in other clonal disorders such as light chain deposition disease and other B cell neoplasms.

How are SFLC measured?

Specimen requests for SFLC at Melbourne Pathology are analysed using the FreeLite™ assay. Polyclonal antibodies in this assay specifically recognise an antigen epitope exposed only when light chains are free in serum and not when they are bound to heavy chains (intact immunoglobulins).

SFLC are quantified by nephelometry using a high-throughput biochemistry analyser. Values for absolute κ and λ light chains and the ratio of κ to λ are reported.

When can SFLC measurement be helpful?

Screening for a plasma cell dyscrasia

In some plasma cell disorders eg. AL amyloidosis and “oligo-secretory” myeloma, serum protein immunofixation electrophoresis (serum IFE) may not detect a paraprotein. SFLC analysis is over 100 times more sensitive than serum IFE in detecting serum light chains².

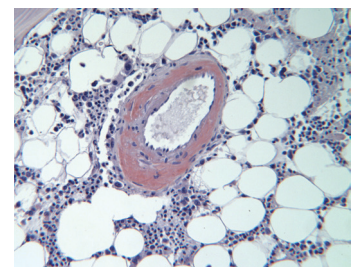
IFE on a 24 hour urine specimen has traditionally been used to detect urinary light chains (Bence Jones proteins) in patients where serum IFE may be negative, but this has limitations. Firstly, FLC do not appear in the urine until the renal absorption capacity is exceeded, leading to a lower sensitivity in detection than if serum light chains were analysed. Secondly, 24 hour urine collection is troublesome and may not be completed correctly which can lead to increased costs and lower compliance with testing.

SFLC can replace urinary IFE in screening for plasma cell disorders with equivalent detection rates when combined with serum IFE³, and is therefore likely to lead to better compliance with testing, with similar costs. In addition two thirds of patients previously classified as “non-secretory myeloma” on the basis of serum/urine IFE, have an abnormal SFLC ratio and are best classified as “oligo-secretory” myeloma.

Prognosis and assessment of response to treatment

An abnormal SFLC ratio at diagnosis has prognostic significance in MGUS, smouldering/symptomatic myeloma, plasmacytoma and AL amyloidosis³.

MGUS patients with a normal SFLC and an IgG paraprotein <15g/L have a very low risk of progression to a symptomatic disorder and may not need regular follow-up⁴.





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SFLC are only recommended as a response marker in AL amyloidosis and myeloma without detectable paraprotein ("oligo-secretory" myeloma)³. Either the absolute value of the involved, or the difference between the involved and uninvolved light chain, should be used to assess response. More severe suppression of the uninvolved light chain is seen with treatment and the SFLC ratio may not reflect the disease burden accurately in this situation. The lack of correlation between paraprotein response and SFLC response in secretory myeloma means SFLC may have normalised when a paraprotein is still detectable by serum IFE⁵. It is not yet known if normalisation of SFLC is always followed by eventual disappearance of the paraprotein (ie. that changes in SFLC always occur before changes in serum IFE). As such SFLC are not currently recommended for use as a response marker in myeloma where a paraprotein is detectable.

What are the limitations of the assay and the results produced?

Due to the nature of the production process for the polyclonal antibodies utilised in the kit, batch-to-batch variation may occur. Although CVs of 10 – 20% have been reported⁶, the manufacturer claims recent improvements in manufacturing processes have reduced this to closer to 5%. Rare cases may occur where the antigen epitopes produced in an individual patient may not be recognised by the antibodies in the kit. Occasionally the antigen excess with extremely high SFLC levels may lead to under-estimation of FLC.

False negative rates when combined with serum IFE are <1%. False-positive results can occur in some clinical situations. Kidney disease can lead to failure of FLC excretion and elevation in total SFLCs, but the ratio of κ to λ should remain unchanged. In inflammatory and infectious disorders, hypergammaglobulinaemia may be associated with an increase in FLC production, but again the ratio of κ to λ should remain unchanged. Examples of SFLC results are shown in Table 1.

The turnaround time for ordering the SFLC test is less than one week.



Dr Duncan Carradice

BMedSc, MBBS, MRCP,
FRACP, FRCPA

Haematology

Dr Carradice graduated from the University of Nottingham, UK in 1996 and completed his haematology training in New Zealand and at the Royal Melbourne Hospital.

He then undertook PhD studies in neutrophil biology and genetics at the Walter and Eliza Hall Institute in the Cancer and Haematology Division.

Dr Carradice joined Melbourne Pathology in 2006, and has an appointment in clinical haematology at Western Hospital, Footscray, in addition to practicing privately.

For further information, please contact Haematology on 9827 7707.

Table 1 – SFLC Results

Total SFLC	SFLC κ/λ ratio	Possible diagnoses
Increased	Normal/Borderline abnormal	Kidney disease. Polyclonal hypergammaglobulinaemia
Increased	Abnormal	Plasma cell dyscrasia
Reduced	Normal	Bone marrow failure
Normal	Normal	Normal result

References

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