

Full Length Research Paper

Comparison of split renal function measured by ^{99m}Tc -DTPA, ^{99m}Tc -MAG3 and ^{99m}Tc -DMSA renal scintigraphies in paediatric age groups

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Currently, in calculation of total and split renal functions (SRF), radionuclide methods are routinely used. We aimed to investigate whether any difference exists between SRF values obtained by ^{99m}Tc -MAG3, ^{99m}Tc -DTPA and ^{99m}Tc -DMSA renal scintigraphies. Retrospectively, 38 patients were included in this study. In Group 1, both ^{99m}Tc -DTPA and ^{99m}Tc -DMSA renal scintigraphies were performed. In Group 2, ^{99m}Tc -MAG3 and ^{99m}Tc -DMSA renal scintigraphies were performed. SRF were calculated by each method and statistically compared with each other. There was no statistically significant difference between SRF values obtained from ^{99m}Tc -DTPA, ^{99m}Tc -MAG3, and ^{99m}Tc -DMSA scintigraphies in 1st and 2nd Group. ^{99m}Tc -DTPA, ^{99m}Tc -MAG3, and ^{99m}Tc -DMSA renal scintigraphies give similar SRF measures which may allow use of either of these techniques for calculating the SRF.

Key words: Kidney split renal function, ^{99m}Tc -DTPA, ^{99m}Tc -MAG3, ^{99m}Tc -DMSA.

INTRODUCTION

Split renal function (SRF), differential renal function, or relative kidney function can be expressed as a percent of total renal function. Information about SRF is very important in patients with unilateral renal disorders and is used to understand sufficient postoperative renal function, otherwise other conditions such as renal replacement therapy must be considered. Before live donor nephrectomy, routine evaluation of SRF is necessary. In some clinical conditions such as unilateral ureteropelvic junction obstruction and other obstructive uropathies, disorders affecting one side of the kidney, etc., follow-up of functional deterioration of diseased kidney is made by SRF.

In determination of SRF, various methods, such as radionuclide methods, triphasic computed tomography

(CT), magnetic resonance imaging (MR) and ultrasound Doppler techniques, etc. can be used (Hackstein et al., 2007; Yura et al., 1991; Daniel, 1999). SRF is traditionally measured by radionuclide renal scintigraphies, using different tracers (Hackstein et al., 2007). ^{99m}Tc -dimercaptosuccinic acid (^{99m}Tc -DMSA) is an agent that is actively taken up by the proximal and distal renal tubular cells, directly from the peritubular vessels, and accumulates in the renal cortex (Miyazaki et al., 2010). This modality is primarily used for imaging functioning cortical mass and individual renal function (Ritchie et al., 2008). It is the most reliable method for assessing chronic cortical scarring (Summerlin et al., 2008) (Figures 1 and 2). ^{99m}Tc -diethylenetriaminepentacetate (^{99m}Tc -DTPA) is an agent that is freely filterable at the glomerulus, but it is neither secreted nor resorbed by the kidney tubules. This method is used to measure total and individual kidney functions. By using the gamma camera technique, glomerular filtration rate (GFR) is calculated for each kidney (Itoh, 2001) (Figure 1).

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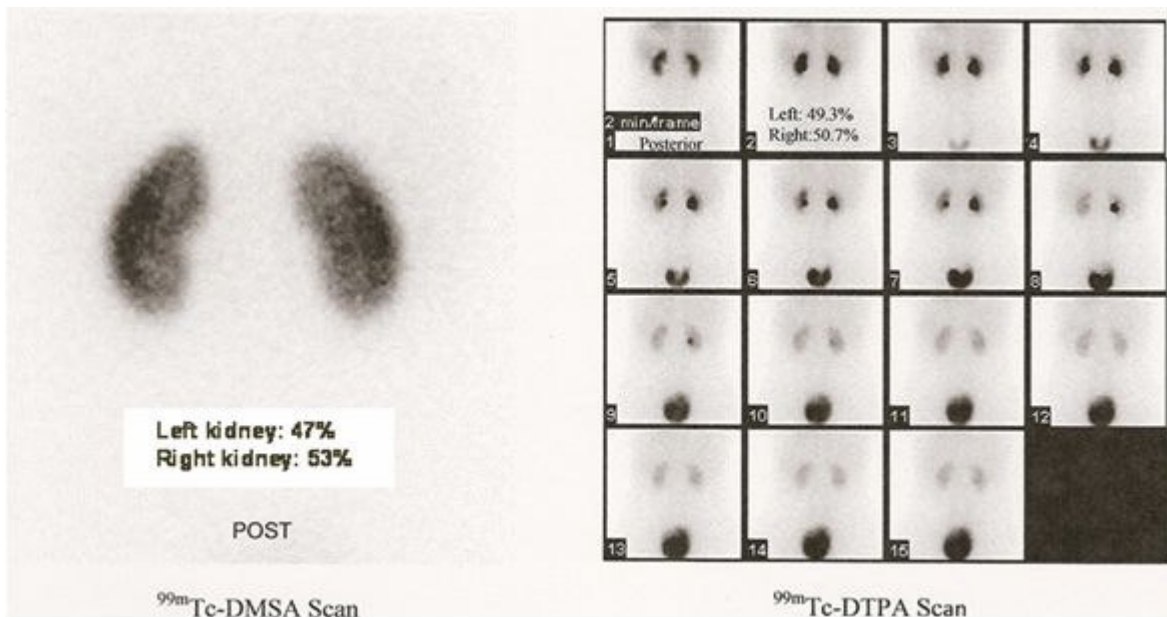


Figure 1. Renal ^{99m}Tc -DMSA and ^{99m}Tc -DTPA scan of a 7-year-old boy with bilateral collecting system dilatation on ultrasonography.

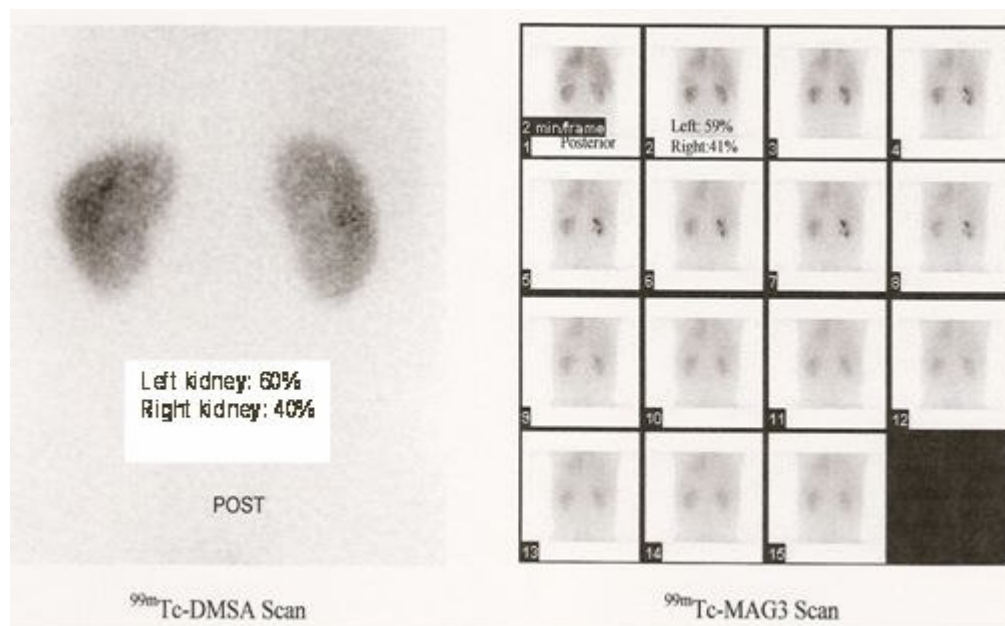


Figure 2. Renal ^{99m}Tc -DMSA and ^{99m}Tc -MAG3 scan of a 9-year-old boy with left collecting system dilatation on ultrasonography and suspicion of renal functional impairment.

^{99m}Tc -mercaptoacetyltriglycine (^{99m}Tc -MAG3) is a renal plasma flow agent almost exclusively excreted by secretion in the proximal tubules and not reabsorbed by the renal tubules. This agent is good for evaluation of renal tubular function (Itoh, 2001). Using a procedure similar to ^{99m}Tc -DTPA scintigraphy, dynamic imaging by gamma camera is obtained. Effective renal plasma flow

(ERPF), reflecting kidney function, is calculated for each kidney (Moran, 1999) (Figure 2).

Another potential renal radiopharmaceutical agent, currently used to measure ERPF and SRF, is ^{99m}Tc -ethylenedicycysteine (^{99m}Tc -EC). It is filtered at the glomerulus and secreted from the proximal tubules (Donoso et al., 2003). The SRF, obtained by using ^{99m}Tc -

Table 1. Split renal functions of left kidneys obtained from ^{99m}Tc -DMSA, ^{99m}Tc -DTPA, and ^{99m}Tc -MAG3 renal scintigraphies.

Method	Left kidney (%)	
	Mean \pm SD	Range
^{99m}Tc -DMSA scan (n = 17)	48.7 \pm 4.4	(35 - 54.4)
^{99m}Tc -DTPA scan (n = 17)	49.6 \pm 3.9	(36 - 53.7)
^{99m}Tc -DMSA scan (n = 21)	49.2 \pm 4.7	(41.2 - 62.7)
^{99m}Tc -MAG3 scan (n = 21)	49.3 \pm 4.1	(42.1 - 59.7)

MAG3, ^{99m}Tc -DTPA and ^{99m}Tc -DMSA renal scintigraphy is currently considered as a robust, accurate and reproducible parameter, provided that it is calculated at a time when no escape of the tracer from the kidney has occurred (Piepsz et al., 1999; Bland and Altman, 1999). We aimed to investigate whether any difference exists between the SRF calculated using ^{99m}Tc -MAG3, ^{99m}Tc -DTPA, and ^{99m}Tc -DMSA renal scintigraphies.

MATERIALS AND METHODS

Retrospectively, 38 patients in paediatric age group, who were referred, from 2008 to 2009, to the Nuclear Medicine Clinics, at the Elazig Research and Training Hospital, for routine indications, such as evaluation of renal parenchymal injury after urinary tract infection, dilated renal collecting system, functional assessment, etc, were included in this study. Patients who did not have renal ultrasonography, or who had insufficient clinical information in their files in our clinical archive, were excluded from the study. In 17 patients, (5 males, 12 females, with a mean age of 8 ± 3.6 years), SRFs were calculated using both ^{99m}Tc -DTPA and ^{99m}Tc -DMSA renal scintigraphies, whereas in 21 patients (4 males, 17 females, with a mean age of 8.3 ± 6.3 years), SRFs were calculated using both ^{99m}Tc -MAG3 and ^{99m}Tc -DMSA renal scintigraphies. The case file, the renal ultrasonography report, and gamma camera imaging data were reviewed for all the cases.

The most common indications for a referral to the Nuclear Medicine Department was urinary tract infection and evaluation of the dilated collecting system. In both groups, radionuclide imaging had been performed within the same week. All radionuclide studies were carried out using a dual-headed GE Infinia Gamma Camera (GE Medical Systems, Milwaukee, WI, USA) equipped with a low-energy, high-resolution collimator. During acquisition, the collimator was set as close as possible to the patient's table.

^{99m}Tc -DTPA scintigraphy

3.7 MBq/kg of ^{99m}Tc -DTPA was injected by IV route. 30 min dynamic imaging, at posterior projection, was performed on 64 x 64 matrix. Using GE Xeleris software, GFR and SRF were calculated according to the gamma camera based method (Bland and Altman, 2003).

^{99m}Tc -MAG3 scintigraphy

1.85 MBq/kg of ^{99m}Tc -MAG3 was injected by IV route. 30 min dynamic imaging, at posterior projection, was performed on 128 x 128 matrix. Using GE Xeleris software, ERPF and SRF were calculated according to the gamma camera based method (Borthne et al., 1999).

^{99m}Tc -DMSA scintigraphy

1.85 MBq/kg of ^{99m}Tc -DMSA was injected by IV route. 2 to 4 h later, static images were acquired at posterior, anterior, and posterior oblique projections for 300 s on a 256 x 256 matrix. Next, SRFs were calculated, semi-automatically, by the geometrical mean of the anterior and posterior images, using GE Xeleris software.

Statistical analysis

SRFs were compared, using the paired student's t-test, in ^{99m}Tc -DTPA/ ^{99m}Tc -DMSA, and ^{99m}Tc -MAG3/ ^{99m}Tc -DMSA groups. In correlation analysis, Pearson's correlation coefficient and regression analysis were used. The Bland-Altman analysis was used to show agreement between the different methods in the measurement of SRF. Statistical analysis was performed using the SPSS 15.0 software program (SPSS Inc., Chicago, Illinois, USA). A p-value of less than 0.05 was considered statistically significant.

RESULTS

SRFs measured by ^{99m}Tc -DTPA, ^{99m}Tc -MAG3, and ^{99m}Tc -DMSA renal scintigraphies are shown in Table 1. There was no statistically significant difference between the split values calculated by two methods, in the ^{99m}Tc -DTPA/ ^{99m}Tc -DMSA and the ^{99m}Tc -MAG3/ ^{99m}Tc -DMSA groups. In correlation analysis, there was a high correlation between the SRF obtained from the ^{99m}Tc -DTPA/ ^{99m}Tc -DMSA and the ^{99m}Tc -MAG3/ ^{99m}Tc -DMSA pairs, for both left and right kidneys ($p < 0.001$ and $r = 0.8$, $r = 0.805$, respectively). Regression and Bland-Altman graphs are shown in Figure 3. In Figure 3b, the mean difference line is below the zero line.

In Figure 3d, mean difference line was located very close to the zero line and considerable amount of difference plots were situated close to the zero line. This means that there is more perfect agreement of the ^{99m}Tc -MAG3 and the ^{99m}Tc -DMSA methods than the ^{99m}Tc -DTPA and ^{99m}Tc -DMSA methods in respect to split renal function calculation.

DISCUSSION

Technetium-99m DMSA scintigraphy is the gold standard for evaluation of SRF (Ritchie et al., 2008). In the

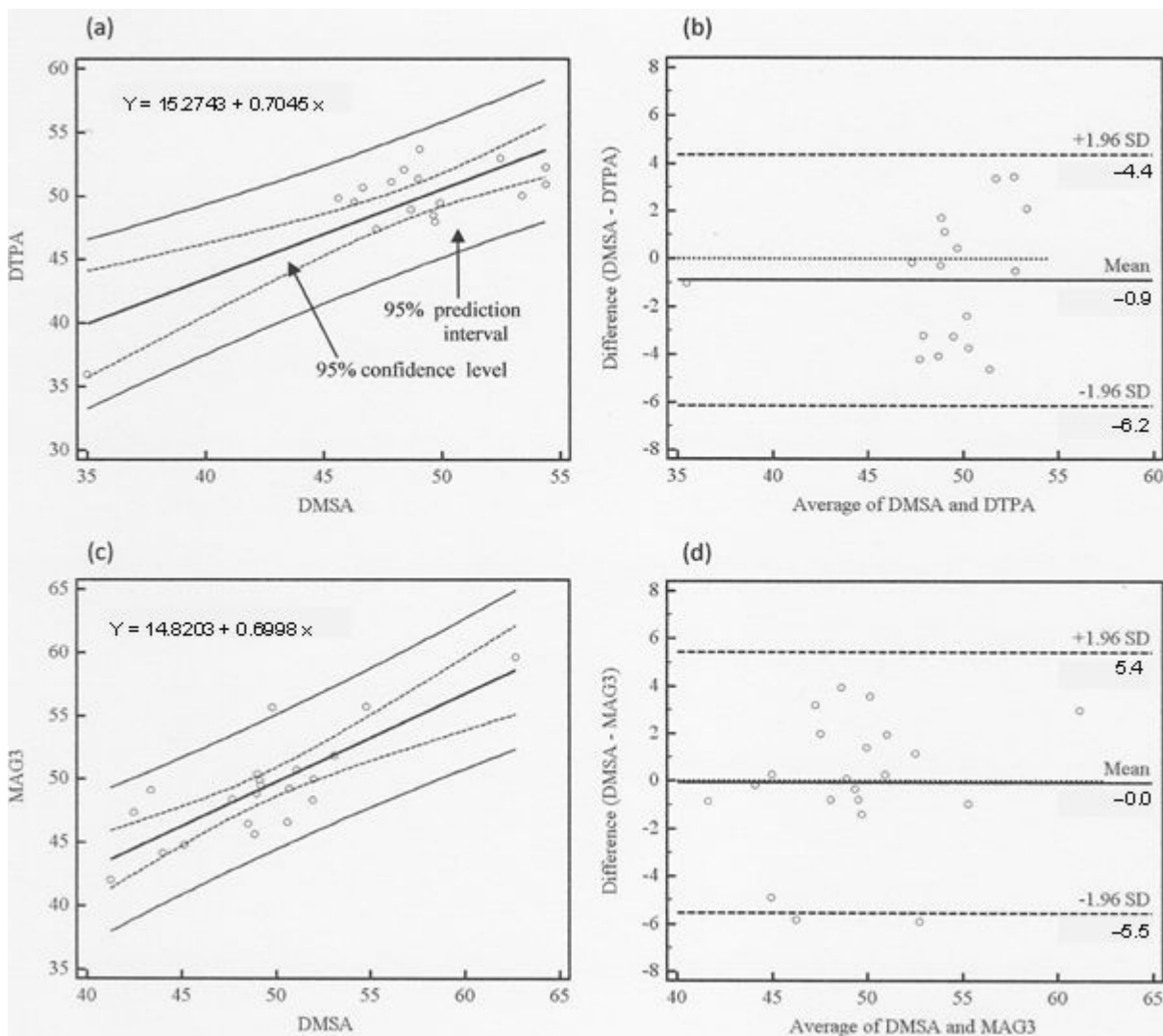


Figure 3. On the left, regression analyses; on the right, Bland-Altman plots between split renal function (%), measured by the ^{99m}Tc -DTPA, ^{99m}Tc -MAG3, and ^{99m}Tc -DMSA renal scintigraphies.

^{99m}Tc -DMSA studies, SRF is calculated using the geometric mean and taking kidney depth into account by acquiring images, anteriorly and posteriorly. In contrast, in ^{99m}Tc -MAG3 and ^{99m}Tc -DTPA studies, SRF is calculated on the images acquired in the posterior position.

^{99m}Tc -DMSA scanning has been regarded as the best method for assessing SRF because the radiotracer is retained, primarily in the proximal convoluted tubules, for a sufficiently long time to allow static imaging of tubular activity which can be performed over several minutes (Summerlin et al., 2008).

This improves the statistical values of a number of counts for a given activity. However, estimation of SRF using ^{99m}Tc -MAG3 and ^{99m}Tc -DTPA must be performed in the first several minutes of a dynamic imaging which usually lasts 20 to 30 min in most centers. Limitation of

the counts, in this way, decreases the statistical value of the measure (Summerlin et al., 2008).

In this study, SRF in the ^{99m}Tc -DTPA/ ^{99m}Tc -DMSA group differs from each other at a rate of 0.9%; and SRF in the ^{99m}Tc -MAG3/ ^{99m}Tc -DMSA group was 0.1% calculated differently in each method. This finding shows that SRF measured by the ^{99m}Tc -MAG3 scintigraphy is more similar to ^{99m}Tc -DMSA scintigraphy than the ^{99m}Tc -DTPA scintigraphy ($p < 0.001$ and $r = 0.8$, $r = 0.805$, respectively) (Figures 3a and c). This may be due to the higher extraction rate of the ^{99m}Tc -MAG3, by the kidneys, than the ^{99m}Tc -DTPA. Statistical analysis showed that the SRF, measured by the ^{99m}Tc -DTPA and the ^{99m}Tc -MAG3 scintigraphy, were not significantly different from the values calculated by the ^{99m}Tc -DMSA renal scintigraphy. In addition to the correlation and regression analysis, we performed a Bland-Altman analysis to demonstrate a

visual representation of the agreement level of the methods (Rohrschneider et al., 2000; Grattan-Smith et al., 2003) (Figures 3b and d).

In the Bland-Altman plot, if two methods are in total agreement, all measured values will be situated on the mean difference line and this line should coincide with the zero line (line of equality). For perfect, but not total, agreement, calculated values are located around the mean line (Rohrschneider et al., 2000). The ^{99m}Tc -DTPA and ^{99m}Tc -DMSA scintigraphic methods, used in the calculation of the SRF in the Bland-Altman plot, showed that the mean difference line was located very close to the zero line (Figure 3b). This indicates perfect agreement of the two methods in the calculation of the SRF. The Bland-Altman plot demonstrated more perfect agreement of the ^{99m}Tc -MAG3 and the ^{99m}Tc -DMSA methods than did the ^{99m}Tc -DTPA and ^{99m}Tc -DMSA methods (Figure 3d). This is because, in the former, the mean difference line almost coincides with the zero line. Furthermore, the values were located closer to the mean difference line in the former than they were in the latter.

Previously, Ritchie et al. (2008) compared SRF values calculated by ^{99m}Tc -DMSA and ^{99m}Tc -MAG3 scintigraphies. They noticed good agreement in calculated SRF values and hypothesized that, in most children there would be no clinically significant difference in the SRF calculated from these two tests. Their study found the mean SRF value of the ^{99m}Tc -MAG3 scintigraphy to be 0.7% different than that of the ^{99m}Tc -DMSA scan. In our study, this difference between methods was 0.1%, which is smaller than their findings. The difference, even this amount, has no clinical importance and may be due to the fact that they included different indications, such as previous pyeloplasty, a duplex collecting system, and partial nephrectomy, which are different parameters than those used in our study. In another study, Miyazaki et al. (2010) found that SRF derived from the ^{99m}Tc -DTPA scintigraphy showed a good correlation with results obtained from the ^{99m}Tc -DMSA scan. They found the mean SRF value of the ^{99m}Tc -DTPA scintigraphy to be 2% different than that of the ^{99m}Tc -DMSA.

In our study, this difference between methods was 0.9%. This small difference between findings may be due to their study's use of an older patient population (median 54 years). Furthermore, their study calculated the SRF, on the posterior view in the ^{99m}Tc -DTPA scintigraphy and SPECT images in the ^{99m}Tc -DMSA scan, whereas our study used posterior images in the ^{99m}Tc -DTPA scintigraphy and the geometric mean of the anterior and posterior images in the ^{99m}Tc -DTPA scan. Traditionally, SFR measurement has been performed by using radionuclide methods. In addition to these methods, there are many different kinds of methods by which SRF can be calculated. The radiological CT technique is one such method. Summerlin et al. (2008) used a 3D model generated from CT angiography for SRF measurement

and compared it with data from the ^{99m}Tc -MAG3 scintigraphy. They found similar SRF values in the CT and the radionuclide methods.

Contrast-enhanced MR imaging (MR urography) has been used in the investigation of urinary tract disorders and renal parenchyma, and in the determination of renal functions, including SRF (Daniel, 1999; Mulligan et al., 1990; Itoh et al., 1996). The potential advantages of MR urography over radionuclide methods are that MR urography has multiplanar capabilities, supplies excellent anatomic resolution and soft tissue contrast, without subjecting the patients to any ionizing radiation. However, technical limitations related to respiratory motion have made MR urography difficult to perform routinely (Itoh et al., 1996). Grattan-Smith et al. (2003) suggested that MR urography was more sensitive than renal scintigraphies in analyzing poorly functioning systems.

The Doppler ultrasound technique has been used to assess the total and split SRF of kidneys (Yura et al., 1991). Yura et al. (1991) compared the SRP estimated by the Doppler ultrasound technique, with that obtained by ^{99m}Tc -DTPA scintigraphy and showed that the SRP value of the Doppler technique correlated well with that of the scintigraphy. They concluded that ultrasonic measurement of renal arterial blood flow by the Doppler method, was useful for assessment of total and split SRF. However, the ultrasonographic method in SRF estimation has not gained routine use, because the radionuclide methods have the advantage of being able to assess renal cortical scarring and drainage of urine as well as renal functions.

As a result, based upon our findings, we have concluded that, regarding the calculation of split renal function, ^{99m}Tc -DTPA, ^{99m}Tc -MAG3, and ^{99m}Tc -DMSA renal scintigraphies can be used reliably and each method gives similar measures. Physicians may use the data obtained from any one of these three modalities, when making decisions with regard to treat their patients in a case that SRF is clinically important.

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