



Renal Function and Associated Laboratory Tests

Contents

Glomerular Filtration Rate (GFR).....	3
Cockcroft-Gault Calculation of Creatinine Clearance	4
Laboratory Reported Calculation of Creatinine Clearance	3
Blood Urea Nitrogen (BUN) to Serum Creatinine (SCr) Ratio	4
Carboplatin Dosing.....	6
GFR and Carboplatin Dosing.....	7

Introduction

Estimation of renal function should be as accurate as possible when treating a patient with drugs that are renally eliminated or potentially nephrotoxic. A renal function assessment should be done prior to the start of cancer drug treatment to ensure that the patient has adequate renal function to eliminate renally cleared drugs. This baseline value also serves as point of reference to which future measurements are compared. Declining renal function may suggest the need for clinical interventions, such as dose modifications, to prevent accumulation of renally eliminated drugs and/or to manage nephrotoxicity. As with all other laboratory tests, it is important to observe the trend rather than a single, isolated measurement.

arsenic	etoposide	methotrexate
bleomycin	fludarabine	mitomycin
capecitabine	gemcitabine	oxaliplatin
CARBOplatin	ifosfamide	pemetrexed
carmustine	lenalidomide	raltitrexed
CISplatin	lomustine	temozolomide
cladribine	melphalan	topotecan
cyclophosphamide		

There is no serum lab test available to quantitatively measure renal function. Instead, the serum tests available assess the concentration of specific proteins that are cleared by the kidneys:

- Serum creatinine (SCr) - a product of muscle breakdown that is filtered by the glomerulus in the kidneys
- Blood urea nitrogen (BUN, urea nitrogen, or urea) - a waste product of protein and amino acid metabolism that accumulates when renal function is reduced

SCr and BUN do not completely represent the renal function status because they can be affected by processes occurring outside the kidneys. The only method to accurately assess kidney function is to measure the Glomerular Filtration Rate (GFR) by nuclear renogram.

Glomerular Filtration Rate (GFR)

Glomerular filtration rate (GFR) is an estimate of the rate that substances, like creatinine, are filtered by the glomerulus. GFR can be used as a proxy measure of renal function. It is most accurately measured with a nuclear renogram (measured GFR). However, as a nuclear renogram involves injection of a renally excreted radioisotope (e.g., ^{99m}Tc-DTPA) and serial imaging of the kidney obtained with a gamma camera to generate a time-activity curve (i.e., renogram), it is not used routinely.

Serum creatinine (SCr) can be used to calculate a creatinine clearance (CrCl) to estimate the GFR. Some limitations include:

- GFR estimates filtration by the glomerulus in the kidneys. A calculated CrCl overestimates GFR because serum creatinine is cleared by glomerular filtration and tubular secretion. A calculated CrCl provides a reasonable estimate of GFR for healthy patients with minimal tubular secretion; it is less accurate (overestimated) for patients with chronic kidney disease with increased tubular secretion.
- Patient weight is a source of inaccuracy, because it does not take into consideration how much of the weight is lean tissue, which is where creatinine is produced. The GFR may be overestimated in patients who are obese or edematous and underestimated in patients with decreased muscle mass.
- Increased exercise can increase creatinine levels resulting in an underestimation of GFR.
- Serum creatinine may increase as much as 50% within 2 hours after a high protein meal and may remain elevated for up to 24 hours.
- Timing of blood samples may affect the GFR calculation because of diurnal variation in serum creatinine, with the peak serum concentration occurring around 7 pm and the nadir in the morning.
- Sudden changes in renal function, such as acute renal failure in hospitalized patients, will not be immediately reflected in the measured SCr.

The accuracy of using a calculated CrCl to estimate GFR is still debated for patients with other conditions such as chronic renal insufficiency, diabetes mellitus, elevated albumin levels, and serum creatinine concentrations less than 10 micromol/L.



See the *Lab Test Interpretation Table*, located below this document on the [Clinical Pharmacy Guide](#) webpage, for examples of normal values and interpretation tips.

Cockcroft-Gault Calculation of Creatinine Clearance

In 1976, Cockcroft and Gault proposed a simple equation that estimated creatinine clearance using the patient's creatinine, age and weight.

BC Cancer uses the modified Cockcroft-Gault equation to calculate creatinine clearance.

Cockcroft-Gault equation:

$$\text{Calculated creatinine clearance (mL/min)} = \frac{N \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum creatinine (micromol/L)}}$$

Where:

N = 1.04 for females

N = 1.23 for males

Laboratory Reported Calculation of Creatinine Clearance

Laboratories also calculate GFR, reported as an estimated glomerular filtration rate (eGFR), when serum creatinine is ordered. A number of recognized formulae have been utilized for this purpose, including the MDRD and CKD-EPI equations.

Blood Urea Nitrogen (BUN) to Serum Creatinine (SCr) Ratio

Comparing the ratio of BUN to SCr can also help provide clues about disease processes that may be the cause of abnormal test results. The BUN:SCr ratio is calculated based on the conventional units (mg/dL) for both BUN and SCr. However, these values are reported in SI units in Canada.

The conversion factors for these values are:

$$\text{BUN mg/dL} = \text{BUN mmol/L} \times 2.8$$



$$\text{Scr mg/dL} = \text{Scr micromol/L} \times 0.01131$$

MediCalc is a website that provides a calculator for determining the BUN to SCr ratio. It will calculate the ratio from SI or conventional units.

Elevated (BUN:SCr > 15:1)

A higher than usual ratio suggests an abnormal process outside the kidneys that interferes with normal kidney function. This can occur either at the point where blood is delivered to the kidney for filtering (prerenal) or at the point where urine leaves the kidneys (postrenal). Although an elevated ratio is considered to be > 15:1, prerenal and postrenal disease usually cause ratios > 20:1. However, a ratio > 20:1 is not clinically significant if both the BUN and SCr are within normal limits.

Prerenal Causes

Delivery of blood to the kidneys for filtering can be impaired by intravascular volume depletion including dehydration, blood loss, and shock. The increase in BUN relative to SCr is due to increased reabsorption of urea that follows sodium and water reabsorption. In cancer patients receiving cancer drugs, common prerenal causes of kidney impairment include vomiting, diarrhea and fever.

Postrenal Causes

Postrenal causes occur when movement of urine from the kidneys is obstructed, which is often due to an enlarged prostate from prostatitis or cancer.

Non-renal Causes

An increased ratio may be the result of increased urea production from a GI bleed, tissue breakdown, or corticosteroid administration. Loss of muscle mass in elderly or chronically ill patients can decrease creatinine production which increases the BUN:SCr ratio. This is a chronic problem and does not explain an acute increase.

Normal (BUN:SCr 10:1 to 15:1)

Disease process within the kidneys (intrarenal or intrinsic causes) usually leads to a normal ratio. Some examples of intrarenal causes include glomerulonephritis, renal tubular disease, pyelonephritis, renal pathology caused by nephrotoxic drugs, severe hypertension, diabetes, arteriosclerosis, cancer, and other disease processes.

A normal ratio can occur in prerenal disease if it is accompanied with decreased urea production as a result of reduced protein intake or liver disease.

Reduced (BUN:SCr < 10:1)

A lower than usual ratio (<10:1) usually suggests decreased urea production as a result of reduced protein intake or liver disease.

Carboplatin Dosing

Assessing renal function plays an important role in determining the optimal dose for carboplatin. The gynecological protocols base carboplatin doses on patient-specific renal function, while most other cytotoxic cancer drugs use body surface area to determine dosage. Examples of carboplatin-containing gynecologic protocols include GOENDCAT and GOOVCARB.

Although carboplatin can be dosed based on BSA, there is poor correlation between BSA and the risk of developing thrombocytopenia; however, there is a strong correlation between total body clearance of carboplatin and GFR, as this drug is mainly eliminated renally.

It has also been shown that the percentage of reduction in platelet count is proportional to the area under the curve (AUC) for carboplatin. In 1989, Calvert and his colleagues proposed a simple equation for optimizing carboplatin dosing based on the AUC, patient-specific GFR, and non-renal elimination. The formula is as follows:

$$\text{Dose} = \text{AUC} \times (\text{GFR} + 25)$$

Where:

Dose = total dose in mg

AUC = desired AUC in mg/mL × min

GFR = glomerular filtration rate*

25 = average non-renal clearance for adults

* GFR is capped at 125 mL/min if it was estimated from a serum creatinine level. The actual GFR can be used if it was measured by nuclear renogram (see GFR and Carboplatin Dosing below)

The AUC depends on the treatment history of the patient. Patients who are chemotherapy-naive may start at an AUC as high as 7; while heavily pretreated patients may start at an AUC of 5, as previous exposure to myelosuppressive

Renal Function Tests

Activation Date: September 2014

Revision Date: August 2020

drugs increases the risk of developing thrombocytopenia by 17%. In order to increase the margin of safety, protocol summaries developed at BC Cancer start with an AUC of 6. Patients with extensive prior radiation therapy, significant cytopenia with prior therapy, or age greater than 80 are usually started with an AUC of 5. Clinical judgment also plays a role in determining the AUC for a treatment course of carboplatin.

Thrombocytopenia is the major dose-limiting side effect of carboplatin, and a platelet count is routinely performed at the nadir between cycles of carboplatin. If there is a decline in platelet count, the carboplatin dose is reduced for subsequent treatment cycles.

Drug tolerability in patients receiving carboplatin is assessed by monitoring the platelet count and serum creatinine. Even when the initial dose is calculated based on a renogram estimate of GFR, serum creatinine is monitored to ensure that renal function is stable throughout the course of treatment. If the serum creatinine increases, this may indicate a decline in renal function. Consult the protocol and general references to determine whether a dose reduction is required. The platelet count is also monitored at the nadir between cycles of carboplatin, and at the beginning of each cycle. The nadir is usually observed at week 3 of a 4 week cycle between doses. Protocols containing carboplatin usually include dose modifications based on the nadir platelet count.

GFR and Carboplatin Dosing

As outlined in the [Glomerular Filtration Rate \(GFR\)](#) section above, a measured GFR (e.g. nuclear renogram) can be ordered if an accurate measure of GFR is required. Typically, the Cockcroft-Gault calculated estimate of GFR or the lab reported estimate of GFR is used to calculate carboplatin dosing. However, if a nuclear renogram was available, this measured clearance would take precedence.

In BC Cancer protocols, the estimated GFR (reported by the lab or calculated using the Cockcroft-Gault equation) is usually capped at 125 mL/min when it is used to calculate an initial carboplatin dose. Note: It is recommended that the same method of estimation be used for calculation of doses throughout a treatment course (i.e. if a lab reported GFR is used initially, dosing for all subsequent cycles should also be based on the lab reported GFR, and not the Cockcroft-Gault estimate).