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(54) Title: METHODS AND COMPOSITIONS FOR DIAGNOSIS AND PROGNOSIS OF RENAL INJURY AND RENAL FAILURE

(57) Abstract: Disclosed are methods and compositions for monitoring, diagnosis, prognosis, and determination of treatment regimens in subjects suffering from or suspected of having a renal injury In particular, disclosed are assays that detect one or more markers selected from the group consisting of Prostatic acid phosphatase, Lactotransfenin, Soluble erythropoietin receptor, Von Willebrand factor, Soluble endothelial protein C receptor, and Beta-2-glycoprotein 1 as diagnostic and prognostic biomarkers in renal injuries.

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METHODS AND COMPOSITIONS FOR DIAGNOSIS AND PROGNOSIS OF RENAL INJURY AND RENAL FAILURE

[0001] The present invention claims priority from U.S. Provisional Patent Applications 61/150,372 filed February 6, 2009; 61/150,374 filed February 6, 2009; 61/150,393 filed February 6, 2009; 61/162,396 filed March 23, 2009; 61/162,402 filed March 23, 2009; and 61/166,333 filed April 3, 2009, each of which is hereby incorporated in its entirety including all tables, figures, and claims.

BACKGROUND OF THE INVENTION

[0002] The following discussion of the background of the invention is merely provided to aid the reader in understanding the invention and is not admitted to describe or constitute prior art to the present invention.

[0003] The kidney is responsible for water and solute excretion from the body. Its functions include maintenance of acid-base balance, regulation of electrolyte concentrations, control of blood volume, and regulation of blood pressure. As such, loss of kidney function through injury and/or disease results in substantial morbidity and mortality. A detailed discussion of renal injuries is provided in Harrison's Principles of Internal Medicine, 17th Ed., McGraw Hill, New York, pages 1741-1830, which are hereby incorporated by reference in their entirety. Renal disease and/or injury may be acute or chronic. Acute and chronic kidney disease are described as follows (from Current Medical Diagnosis & Treatment 2008, 47th Ed, McGraw Hill, New York, pages 785-815, which are hereby incorporated by reference in their entirety): "Acute renal failure is worsening of renal function over hours to days, resulting in the retention of nitrogenous wastes (such as urea nitrogen) and creatinine in the blood. Retention of these substances is called azotemia. Chronic renal failure (chronic kidney disease) results from an abnormal loss of renal function over months to years".

[0004] Acute renal failure (ARF, also known as acute kidney injury, or AKI) is an abrupt (typically detected within about 48 hours to 1 week)reduction in glomerular filtration. This loss of filtration capacity results in retention of nitrogenous (urea and creatinine) and non-nitrogenous waste products that are normally excreted by the kidney, a reduction in urine output, or both. It is reported that ARF complicates about 5% of hospital admissions, 4-15% of cardiopulmonary bypass surgeries, and up to 30% of

intensive care admissions. ARF may be categorized as prerenal, intrinsic renal, or postrenal in causation. Intrinsic renal disease can be further divided into glomerular, tubular, interstitial, and vascular abnormalities. Major causes of ARF are described in the following table, which is adapted from the Merck Manual, 17th ed., Chapter 222, and which is hereby incorporated by reference in their entirety:

Type	Risk Factors
Prerenal	
ECF volume depletion	Excessive diuresis, hemorrhage, GI losses, loss of intravascular fluid into the extravascular space (due to ascites, peritonitis, pancreatitis, or burns), loss of skin and mucus membranes, renal salt- and water-wasting states
Low cardiac output	Cardiomyopathy, MI, cardiac tamponade, pulmonary embolism, pulmonary hypertension, positive-pressure mechanical ventilation
Low systemic vascular resistance	Septic shock, liver failure, antihypertensive drugs
Increased renal vascular resistance	NSAIDs, cyclosporines, tacrolimus, hypercalcemia, anaphylaxis, anesthetics, renal artery obstruction, renal vein thrombosis, sepsis, hepatorenal syndrome
Decreased efferent arteriolar tone (leading to decreased GFR from reduced glomerular transcapillary pressure, especially in patients with bilateral renal artery stenosis)	ACE inhibitors or angiotensin II receptor blockers
Intrinsic Renal	
Acute tubular injury	Ischemia (prolonged or severe prerenal state): surgery, hemorrhage, arterial or venous obstruction; Toxins: NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, streptozotocin
Acute glomerulonephritis	ANCA-associated: Crescentic glomerulonephritis, polyarteritis nodosa, Wegener's granulomatosis; Anti-GBM glomerulonephritis: Goodpasture's syndrome; Immune-complex: Lupus glomerulonephritis, postinfectious glomerulonephritis, cryoglobulinemic glomerulonephritis
Acute tubulointerstitial nephritis	Drug reaction (eg, β-lactams, NSAIDs, sulfonamides, ciprofloxacin, thiazide diuretics, furosemide, phenytoin, allopurinol, pyelonephritis, papillary necrosis
Acute vascular nephropathy	Vasculitis, malignant hypertension, thrombotic microangiopathies, scleroderma, atheroembolism
Infiltrative diseases	Lymphoma, sarcoidosis, leukemia

Postrenal	
Tubular precipitation	Uric acid (tumor lysis), sulfonamides, triamterene, acyclovir, indinavir, methotrexate, ethylene glycol ingestion, myeloma protein, myoglobin
Ureteral obstruction	Intrinsic: Calculi, clots, sloughed renal tissue, fungus ball, edema, malignancy, congenital defects; Extrinsic: Malignancy, retroperitoneal fibrosis, ureteral trauma during surgery or high impact injury
Bladder obstruction	Mechanical: Benign prostatic hyperplasia, prostate cancer, bladder cancer, urethral strictures, phimosis, paraphimosis, urethral valves, obstructed indwelling urinary catheter; Neurogenic: Anticholinergic drugs, upper or lower motor neuron lesion

[0005] In the case of ischemic ARF, the course of the disease may be divided into four phases. During an initiation phase, which lasts hours to days, reduced perfusion of the kidney is evolving into injury. Glomerular ultrafiltration reduces, the flow of filtrate is reduced due to debris within the tubules, and back leakage of filtrate through injured epithelium occurs. Renal injury can be mediated during this phase by reperfusion of the kidney. Initiation is followed by an extension phase which is characterized by continued ischemic injury and inflammation and may involve endothelial damage and vascular congestion. During the maintenance phase, lasting from 1 to 2 weeks, renal cell injury occurs, and glomerular filtration and urine output reaches a minimum. A recovery phase can follow in which the renal epithelium is repaired and GFR gradually recovers. Despite this, the survival rate of subjects with ARF may be as low as about 60%.

[0006] Acute kidney injury caused by radiocontrast agents (also called contrast media) and other nephrotoxins such as cyclosporine, antibiotics including aminoglycosides and anticancer drugs such as cisplatin manifests over a period of days to about a week. Contrast induced nephropathy (CIN, which is AKI caused by radiocontrast agents) is thought to be caused by intrarenal vasoconstriction (leading to ischemic injury) and from the generation of reactive oxygen species that are directly toxic to renal tubular epithelial cells. CIN classically presents as an acute (onset within 24-48h) but reversible (peak 3-5 days, resolution within 1 week) rise in blood urea nitrogen and serum creatinine.

[0007] A commonly reported criteria for defining and detecting AKI is an abrupt (typically within about 2-7 days or within a period of hospitalization) elevation of serum creatinine. Although the use of serum creatinine elevation to define and detect AKI is

well established, the magnitude of the serum creatinine elevation and the time over which it is measured to define AKI varies considerably among publications. Traditionally, relatively large increases in serum creatinine such as 100%, 200%, an increase of at least 100% to a value over 2 mg/dL and other definitions were used to define AKI. However, the recent trend has been towards using smaller serum creatinine rises to define AKI. The relationship between serum creatinine rise, AKI and the associated health risks are reviewed in Praught and Shlipak, *Curr Opin Nephrol Hypertens* 14:265-270, 2005 and Chertow et al, *J Am Soc Nephrol* 16: 3365-3370, 2005, which, with the references listed therein, are hereby incorporated by reference in their entirety. As described in these publications, acute worsening renal function (AKI) and increased risk of death and other detrimental outcomes are now known to be associated with very small increases in serum creatinine. These increases may be determined as a relative (percent) value or a nominal value. Relative increases in serum creatinine as small as 20% from the pre-injury value have been reported to indicate acutely worsening renal function (AKI) and increased health risk, but the more commonly reported value to define AKI and increased health risk is a relative increase of at least 25%. Nominal increases as small as 0.3 mg/dL, 0.2 mg/dL or even 0.1 mg/dL have been reported to indicate worsening renal function and increased risk of death. Various time periods for the serum creatinine to rise to these threshold values have been used to define AKI, for example, ranging from 2 days, 3 days, 7 days, or a variable period defined as the time the patient is in the hospital or intensive care unit. These studies indicate there is not a particular threshold serum creatinine rise (or time period for the rise) for worsening renal function or AKI, but rather a continuous increase in risk with increasing magnitude of serum creatinine rise.

[0008] One study (Lassnigg et all, J Am Soc Nephrol 15:1597-1605, 2004, hereby incorporated by reference in its entirety) investigated both increases and decreases in serum creatinine. Patients with a mild fall in serum creatinine of -0.1 to -0.3 mg/dL following heart surgery had the lowest mortality rate. Patients with a larger fall in serum creatinine (more than or equal to -0.4 mg/dL) or any increase in serum creatinine had a larger mortality rate. These findings caused the authors to conclude that even very subtle changes in renal function (as detected by small creatinine changes within 48 hours of surgery) seriously effect patient's outcomes. In an effort to reach consensus on a unified classification system for using serum creatinine to define AKI in clinical trials and in clinical practice, Bellomo *et al., Crit Care*. 8(4):R204-12, 2004, which is hereby

incorporated by reference in its entirety, proposes the following classifications for stratifying AKI patients:

"Risk": serum creatinine increased 1.5 fold from baseline OR urine production of <0.5 ml/kg body weight/hr for 6 hours;

"Injury": serum creatinine increased 2.0 fold from baseline OR urine production <0.5 ml/kg/hr for 12 h;

"Failure": serum creatinine increased 3.0 fold from baseline OR creatinine >355 μmol/l (with a rise of >44) or urine output below 0.3 ml/kg/hr for 24 h or anuria for at least 12 hours;

And included two clinical outcomes:

"Loss": persistent need for renal replacement therapy for more than four weeks.

"ESRD": end stage renal disease—the need for dialysis for more than 3 months.

These criteria are called the RIFLE criteria, which provide a useful clinical tool to classify renal status. As discussed in Kellum, *Crit. Care Med.* 36: S141-45, 2008 and Ricci *et al., Kidney Int.* 73, 538-546, 2008, each hereby incorporated by reference in its entirety, the RIFLE criteria provide a uniform definition of AKI which has been validated in numerous studies.

[0009] More recently, Mehta *et al., Crit. Care* 11:R31 (doi:10.1186.cc5713), 2007, hereby incorporated by reference in its entirety, proposes the following similar classifications for stratifying AKI patients, which have been modified from RIFLE:

"Stage I": increase in serum creatinine of more than or equal to 0.3 mg/dL (≥ 26.4 μmol/L) or increase to more than or equal to 150% (1.5-fold) from baseline OR urine output less than 0.5 mL/kg per hour for more than 6 hours;

"Stage II": increase in serum creatinine to more than 200% (> 2-fold) from baseline OR urine output less than 0.5 mL/kg per hour for more than 12 hours;

"Stage III": increase in serum creatinine to more than 300% (> 3-fold) from baseline OR serum creatinine ≥ 354 μmol/L accompanied by an acute increase of at least 44 μmol/L OR urine output less than 0.3 mL/kg per hour for 24 hours or anuria for 12 hours.

[0010] The CIN Consensus Working Panel (McCollough et al, Rev Cardiovasc Med. *2006;7(4):177-197,* hereby incorporated by reference in its entirety*)* uses a serum

creatinine rise of 25% to define Contrast induced nephropathy (which is a type of AKI).Although various groups propose slightly different criteria for using serum creatinine to detect AKI, the consensus is that small changes in serum creatinine, such as 0.3 mg/dL or 25%, are sufficient to detect AKI (worsening renal function) and that the magnitude of the serum creatinine change is an indicator of the severity of the AKI and mortality risk.

[0011] Although serial measurement of serum creatinine over a period of days is an accepted method of detecting and diagnosing AKI and is considered one of the most important tools to evaluate AKI patients, serum creatinine is generally regarded to have several limitations in the diagnosis, assessment and monitoring of AKI patients. The time period for serum creatinine to rise to values (e.g., a 0.3 mg/dL or 25% rise) considered diagnostic for AKI can be 48 hours or longer depending on the definition used. Since cellular injury in AKI can occur over a period of hours, serum creatinine elevations detected at 48 hours or longer can be a late indicator of injury, and relying on serum creatinine can thus delay diagnosis of AKI. Furthermore, serum creatinine is not a good indicator of the exact kidney status and treatment needs during the most acute phases of AKI when kidney function is changing rapidly. Some patients with AKI will recover fully, some will need dialysis (either short term or long term) and some will have other detrimental outcomes including death, major adverse cardiac events and chronic kidney disease. Because serum creatinine is a marker of filtration rate, it does not differentiate between the causes of AKI (pre-renal, intrinsic renal, post-renal obstruction, atheroembolic, etc) or the category or location of injury in intrinsic renal disease (for example, tubular, glomerular or interstitial in origin). Urine output is similarly limited, Knowing these things can be of vital importance in managing and treating patients with AKI.

[0012] These limitations underscore the need for better methods to detect and assess AKI, particularly in the early and subclinical stages, but also in later stages when recovery and repair of the kidney can occur. Furthermore, there is a need to better identify patients who are at risk of having an AKI.

BRIEF SUMMARY OF THE INVENTION

[0013] In one aspect, the invention provides methods and compositions for evaluating renal function in a subject. As described herein, measurement of one or more markers

selected from the group consisting of Prostatic acid phosphatase, Lactotransferrin, Soluble erythropoietin receptor, Von Willebrand factor, Soluble endothelial protein C receptor, and Beta-2-glycoprotein 1 (collectively referred to herein as "kidney injury markers, and individually as a "kidney injury marker") can be used for diagnosis, prognosis, risk stratification, staging, monitoring, categorizing and determination of further diagnosis and treatment regimens in subjects suffering or at risk of suffering from an injury to renal function, reduced renal function, and/or acute renal failure (also called acute kidney injury).

[0014] These kidney injury markers may be used, individually or in panels comprising a plurality of kidney injury markers, for risk stratification (that is, to identify subjects at risk for a future injury to renal function, for future progression to reduced renal function, for future progression to ARF, for future improvement in renal function, *etc.*); for diagnosis of existing disease (that is, to identify subjects who have suffered an injury to renal function, who have progressed to reduced renal function, who have progressed to ARF, *etc.*); for monitoring for deterioration or improvement of renal function; and for predicting a future medical outcome, such as improved or worsening renal function, a decreased or increased mortality risk, a decreased or increased risk that a subject will require renal replacement therapy (*i.e.*, hemodialysis, peritoneal dialysis, hemofiltration, and/or renal transplantation, a decreased or increased risk that a subject will recover from an injury to renal function, a decreased or increased risk that a subject will recover from ARF, a decreased or increased risk that a subject will progress to end stage renal disease, a decreased or increased risk that a subject will progress to chronic renal failure, a decreased or increased risk that a subject will suffer rejection of a transplanted kidney, *etc.*

[0015] In another aspect, the present invention relates to methods for evaluating renal status in a subject. These methods comprise performing an assay method that is configured to detect one or more kidney injury markers of the present invention in a body fluid sample obtained from the subject. The assay result(s), for example a measured concentration of one or more markers selected from the group consisting of Prostatic acid phosphatase, Lactotransferrin, Soluble erythropoietin receptor, Von Willebrand factor, Soluble endothelial protein C receptor, and Beta-2-glycoprotein 1 is/are then correlated to the renal status of the subject. This correlation to renal status may include correlating the assay result(s) to one or more of risk stratification, diagnosis, prognosis, staging,

classifying and monitoring of the subject as described herein. Thus, the present invention utilizes one or more kidney injury markers of the present invention for the evaluation of renal injury.

[0015A] In another aspect, the present invention provides a method for evaluating renal status in a subject that is not the recipient of a transplant, comprising:

performing one or more assays configured to detect one or more kidney injury marker(s) in a body fluid sample obtained from the subject to provide an assay result(s), wherein at least one of said markers is Soluble endothelial protein C receptor;

determining an assay result(s) for each assay comprising a measured concentration of one or more kidney injury marker(s); and

correlating the assay result(s) to one or more of risk stratification, staging, prognosis, classifying and monitoring of the renal status of the subject,

wherein said correlating step comprises assigning a likelihood of one or more future changes in renal status to the subject based on the assay result(s).

[0016] In certain embodiments, the methods for evaluating renal status described herein are methods for risk stratification of the subject; that is, assigning a likelihood of one or more future changes in renal status to the subject. In these embodiments, the assay result(s) is/are correlated to one or more such future changes. The following are preferred risk stratification embodiments.

[0017] In preferred risk stratification embodiments, these methods comprise determining a subject's risk for a future injury to renal function, and the assay result(s) is/are correlated to a likelihood of such a future injury to renal function. For example, the measured concentration(s) may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of suffering a future injury to renal function is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold. For a "negative going" kidney injury marker, an increased likelihood of suffering a future injury to renal function is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold.

[0018] In other preferred risk stratification embodiments, these methods comprise determining a subject's risk for future reduced renal function, and the assay result(s)

is/are correlated to a likelihood of such reduced renal function. For example, the measured concentrations may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of suffering a future reduced renal function is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold. For a "negative going" kidney injury marker, an increased likelihood of future reduced renal function is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold.

[0019] In still other preferred risk stratification embodiments, these methods comprise determining a subject's likelihood for a future improvement in renal function, and the

assay result(s) is/are correlated to a likelihood of such a future improvement in renal function. For example, the measured concentration(s) may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of a future improvement in renal function is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold. For a "negative going" kidney injury marker, an increased likelihood of a future improvement in renal function is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold.

[0020] In yet other preferred risk stratification embodiments, these methods comprise determining a subject's risk for progression to ARF, and the result(s) is/are correlated to a likelihood of such progression to ARF. For example, the measured concentration(s) may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of progression to ARF is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold. For a "negative going" kidney injury marker, an increased likelihood of progression to ARF is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold.

[0021] And in other preferred risk stratification embodiments, these methods comprise determining a subject's outcome risk, and the assay result(s) is/are correlated to a likelihood of the occurrence of a clinical outcome related to a renal injury suffered by the subject. For example, the measured concentration(s) may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of one or more of: acute kidney injury, progression to a worsening stage of AKI, mortality, a requirement for renal replacement therapy, a requirement for withdrawal of renal toxins, end stage renal disease, heart failure, stroke, myocardial infarction, progression to chronic kidney disease, *etc*., is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold. For a "negative going" kidney injury marker, an increased likelihood of one or more of: acute kidney injury, progression to a worsening stage of AKI, mortality, a requirement for renal replacement therapy, a requirement for withdrawal of renal toxins, end stage renal disease, heart failure, stroke, myocardial infarction, progression to chronic

kidney disease, *etc.*, is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold.

[0022] In such risk stratification embodiments, preferably the likelihood or risk assigned is that an event of interest is more or less likely to occur within 180 days of the time at which the body fluid sample is obtained from the subject. In particularly preferred embodiments, the likelihood or risk assigned relates to an event of interest occurring within a shorter time period such as 18 months, 120 days, 90 days, 60 days, 45 days, 30 days, 21 days, 14 days, 7 days, 5 days, 96 hours, 72 hours, 48 hours, 36 hours, 24 hours, 12 hours, or less. A risk at 0 hours of the time at which the body fluid sample is obtained from the subject is equivalent to diagnosis of a current condition.

[0023] In preferred risk stratification embodiments, the subject is selected for risk stratification based on the pre-existence in the subject of one or more known risk factors for prerenal, intrinsic renal, or postrenal ARF. For example, a subject undergoing or having undergone major vascular surgery, coronary artery bypass, or other cardiac surgery; a subject having pre-existing congestive heart failure, preeclampsia, eclampsia, diabetes mellitus, hypertension, coronary artery disease, proteinuria, renal insufficiency, glomerular filtration below the normal range, cirrhosis, serum creatinine above the normal range, or sepsis; or a subject exposed to NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, or streptozotocin are all preferred subjects for monitoring risks according to the methods described herein. This list is not meant to be limiting. By "pre-existence" in this context is meant that the risk factor exists at the time the body fluid sample is obtained from the subject. In particularly preferred embodiments, a subject is chosen for risk stratification based on an existing diagnosis of injury to renal function, reduced renal function, or ARF.

[0024] In other embodiments, the methods for evaluating renal status described herein are methods for diagnosing a renal injury in the subject; that is, assessing whether or not a subject has suffered from an injury to renal function, reduced renal function, or ARF. In these embodiments, the assay result(s), for example a measured concentration of one or more markers selected from the group consisting of Prostatic acid phosphatase, Lactotransferrin, Soluble erythropoietin receptor, Von Willebrand factor, Soluble endothelial protein C receptor, and Beta-2-glycoprotein 1 is/are correlated to the

occurrence or nonoccurrence of a change in renal status. The following are preferred diagnostic embodiments.

[0025] In preferred diagnostic embodiments, these methods comprise diagnosing the occurrence or nonoccurrence of an injury to renal function, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of such an injury. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of an injury to renal function is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of an injury to renal function may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of an injury to renal function is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration is above the threshold); alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of an injury to renal function may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

[0026] In other preferred diagnostic embodiments, these methods comprise diagnosing the occurrence or nonoccurrence of reduced renal function, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of an injury causing reduced renal function. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of an injury causing reduced renal function is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of an injury causing reduced renal function may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of an injury causing reduced renal function is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration

is above the threshold); alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of an injury causing reduced renal function may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

[0027] In yet other preferred diagnostic embodiments, these methods comprise diagnosing the occurrence or nonoccurrence of ARF, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of an injury causing ARF. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of ARF is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of ARF may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of ARF is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration is above the threshold); alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of ARF may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

[0028] In still other preferred diagnostic embodiments, these methods comprise diagnosing a subject as being in need of renal replacement therapy, and the assay result(s) is/are correlated to a need for renal replacement therapy. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of an injury creating a need for renal replacement therapy is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of an injury creating a need for renal replacement therapy may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of an injury creating a need for renal replacement therapy is assigned to the subject when the measured concentration is below

the threshold (relative to the likelihood assigned when the measured concentration is above the threshold); alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of an injury creating a need for renal replacement therapy may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

[0029] In still other preferred diagnostic embodiments, these methods comprise diagnosing a subject as being in need of renal transplantation, and the assay result(s0 is/are correlated to a need for renal transplantation. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of an injury creating a need for renal transplantation is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of an injury creating a need for renal transplantation may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of an injury creating a need for renal transplantation is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration is above the threshold); alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of an injury creating a need for renal transplantation may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

[0030] In still other embodiments, the methods for evaluating renal status described herein are methods for monitoring a renal injury in the subject; that is, assessing whether or not renal function is improving or worsening in a subject who has suffered from an injury to renal function, reduced renal function, or ARF. In these embodiments, the assay result(s), for example a measured concentration of one or more markers selected from the group consisting of Prostatic acid phosphatase, Lactotransferrin, Soluble erythropoietin receptor, Von Willebrand factor, Soluble endothelial protein C receptor, and Beta-2-glycoprotein 1 is/are correlated to the occurrence or nonoccurrence of a change in renal status. The following are preferred monitoring embodiments.

[0031] In preferred monitoring embodiments, these methods comprise monitoring renal status in a subject suffering from an injury to renal function, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of a change in renal status in the subject. For example, the measured concentration(s) may be compared to a threshold value. For a positive going marker, when the measured concentration is above the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is below the threshold, an improvement of renal function may be assigned to the subject. For a negative going marker, when the measured concentration is below the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is above the threshold, an improvement of renal function may be assigned to the subject.

[0032] In other preferred monitoring embodiments, these methods comprise monitoring renal status in a subject suffering from reduced renal function, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of a change in renal status in the subject. For example, the measured concentration(s) may be compared to a threshold value. For a positive going marker, when the measured concentration is above the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is below the threshold, an improvement of renal function may be assigned to the subject. For a negative going marker, when the measured concentration is below the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is above the threshold, an improvement of renal function may be assigned to the subject.

[0033] In yet other preferred monitoring embodiments, these methods comprise monitoring renal status in a subject suffering from acute renal failure, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of a change in renal status in the subject. For example, the measured concentration(s) may be compared to a threshold value. For a positive going marker, when the measured concentration is above the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is below the threshold, an improvement of renal function may be assigned to the subject. For a negative going marker, when the measured concentration is below the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is above the threshold, an improvement of renal function may be assigned to the subject.

[0034] In other additional preferred monitoring embodiments, these methods comprise monitoring renal status in a subject at risk of an injury to renal function due to the pre-existence of one or more known risk factors for prerenal, intrinsic renal, or postrenal ARF, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of a change in renal status in the subject. For example, the measured concentration(s) may be compared to a threshold value. For a positive going marker, when the measured concentration is above the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is below the threshold, an improvement of renal function may be assigned to the subject. For a negative going marker, when the measured concentration is below the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is above the threshold, an improvement of renal function may be assigned to the subject.

[0035] In still other embodiments, the methods for evaluating renal status described herein are methods for classifying a renal injury in the subject; that is, determining whether a renal injury in a subject is prerenal, intrinsic renal, or postrenal; and/or further subdividing these classes into subclasses such as acute tubular injury, acute glomerulonephritis acute tubulointerstitial nephritis, acute vascular nephropathy, or infiltrative disease; and/or assigning a likelihood that a subject will progress to a particular RIFLE stage. In these embodiments, the assay result(s), for example a measured concentration of one or more markers selected from the group consisting of Prostatic acid phosphatase, Lactotransferrin, Soluble erythropoietin receptor, Von Willebrand factor, Soluble endothelial protein C receptor, and Beta-2-glycoprotein 1 is/are correlated to a particular class and/or subclass. The following are preferred classification embodiments.

[0036] In preferred classification embodiments, these methods comprise determining whether a renal injury in a subject is prerenal, intrinsic renal, or postrenal; and/or further subdividing these classes into subclasses such as acute tubular injury, acute glomerulonephritis acute tubulointerstitial nephritis, acute vascular nephropathy, or infiltrative disease; and/or assigning a likelihood that a subject will progress to a particular RIFLE stage, and the assay result(s) is/are correlated to the injury classification for the subject. For example, the measured concentration may be compared to a threshold value, and when the measured concentration is above the threshold, a particular

classification is assigned; alternatively, when the measured concentration is below the threshold, a different classification may be assigned to the subject.

[0037] A variety of methods may be used by the skilled artisan to arrive at a desired threshold value for use in these methods. For example, the threshold value may be determined from a population of normal subjects by selecting a concentration representing the 75th, 85th, 90th, 95th, or 99th percentile of a kidney injury marker measured in such normal subjects. Alternatively, the threshold value may be determined from a "diseased" population of subjects, e.g., those suffering from an injury or having a predisposition for an injury (e.g., progression to ARF or some other clinical outcome such as death, dialysis, renal transplantation, *etc.*), by selecting a concentration representing the 75th, 85th, 90th, 95th, or 99th percentile of a kidney injury marker measured in such subjects. In another alternative, the threshold value may be determined from a prior measurement of a kidney injury marker in the same subject; that is, a temporal change in the level of a kidney injury marker in the subject may be used to assign risk to the subject.

[001] The foregoing discussion is not meant to imply, however, that the kidney injury markers of the present invention must be compared to corresponding individual thresholds. Methods for combining assay results can comprise the use of multivariate logistical regression, loglinear modeling, neural network analysis, n-of-m analysis, decision tree analysis, calculating ratios of markers, *etc.* This list is not meant to be limiting. In these methods, a composite result which is determined by combining individual markers may be treated as if it is itself a marker; that is, a threshold may be determined for the composite result as described herein for individual markers, and the composite result for an individual patient compared to this threshold.

[0038] The ability of a particular test to distinguish two populations can be established using ROC analysis. For example, ROC curves established from a "first" subpopulation which is predisposed to one or more future changes in renal status, and a "second" subpopulation which is not so predisposed can be used to calculate a ROC curve, and the area under the curve provides a measure of the quality of the test. Preferably, the tests described herein provide a ROC curve area greater than 0.5, preferably at least 0.6, more preferably 0.7, still more preferably at least 0.8, even more preferably at least 0.9, and most preferably at least 0.95.

[0039] In certain aspects, the measured concentration of one or more kidney injury markers, or a composite of such markers, may be treated as continuous variables. For example, any particular concentration can be converted into a corresponding probability of a future reduction in renal function for the subject, the occurrence of an injury, a classification, etc. In yet another alternative, a threshold that can provide an acceptable level of specificity and sensitivity in separating a population of subjects into "bins" such as a "first" subpopulation (e.g., which is predisposed to one or more future changes in renal status, the occurrence of an injury, a classification, etc.) and a "second" subpopulation which is not so predisposed. A threshold value is selected to separate this first and second population by one or more of the following measures of test accuracy:

an odds ratio greater than 1, preferably at least about 2 or more or about 0.5 or less, more preferably at least about 3 or more or about 0.33 or less, still more preferably at least about 4 or more or about 0.25 or less, even more preferably at least about 5 or more or about 0.2 or less, and most preferably at least about 10 or more or about 0.1 or less;

a specificity of greater than 0.5, preferably at least about 0.6, more preferably at least about 0.7, still more preferably at least about 0.8, even more preferably at least about 0.9 and most preferably at least about 0.95, with a corresponding sensitivity greater than 0.2, preferably greater than about 0.3, more preferably greater than about 0.4, still more preferably at least about 0.5, even more preferably about 0.6, yet more preferably greater than about 0.7, still more preferably greater than about 0.8, more preferably greater than about 0.9, and most preferably greater than about 0.95;

a sensitivity of greater than 0.5, preferably at least about 0.6, more preferably at least about 0.7, still more preferably at least about 0.8, even more preferably at least about 0.9 and most preferably at least about 0.95, with a corresponding specificity greater than 0.2, preferably greater than about 0.3, more preferably greater than about 0.4, still more preferably at least about 0.5, even more preferably about 0.6, yet more preferably greater than about 0.7, still more preferably greater than about 0.8, more preferably greater than about 0.9, and most preferably greater than about 0.95;

at least about 75% sensitivity, combined with at least about 75% specificity;

a positive likelihood ratio (calculated as sensitivity/(1-specificity)) of greater than 1, at least about 2, more preferably at least about 3, still more preferably at least about 5, and most preferably at least about 10; or

a negative likelihood ratio (calculated as (1-sensitivity)/specificity) of less than 1, less than or equal to about 0.5, more preferably less than or equal to about 0.3, and most preferably less than or equal to about 0.1.

The term "about" in the context of any of the above measurements refers to +/- 5% of a given measurement.

[0040] Multiple thresholds may also be used to assess renal status in a subject. For example, a "first" subpopulation which is predisposed to one or more future changes in renal status, the occurrence of an injury, a classification, etc., and a "second" subpopulation which is not so predisposed can be combined into a single group. This group is then subdivided into three or more equal parts (known as tertiles, quartiles, quintiles, etc., depending on the number of subdivisions). An odds ratio is assigned to subjects based on which subdivision they fall into. If one considers a tertile, the lowest or highest tertile can be used as a reference for comparison of the other subdivisions. This reference subdivision is assigned an odds ratio of 1. The second tertile is assigned an odds ratio that is relative to that first tertile. That is, someone in the second tertile might be 3 times more likely to suffer one or more future changes in renal status in comparison to someone in the first tertile. The third tertile is also assigned an odds ratio that is relative to that first tertile.

[0041] In certain embodiments, the assay method is an immunoassay. Antibodies for use in such assays will specifically bind a full length kidney injury marker of interest, and may also bind one or more polypeptides that are "related" thereto, as that term is defined hereinafter. Numerous immunoassay formats are known to those of skill in the art. Preferred body fluid samples are selected from the group consisting of urine, blood, serum, saliva, tears, and plasma.

[0042] The foregoing method steps should not be interpreted to mean that the kidney injury marker assay result(s) is/are used in isolation in the methods described herein. Rather, additional variables or other clinical indicia may be included in the methods described herein. For example, a risk stratification, diagnostic, classification, monitoring, etc. method may combine the assay result(s) with one or more variables measured for the subject selected from the group consisting of demographic information (e.g., weight, sex, age, race), medical history (e.g., family history, type of surgery, pre-existing disease such as aneurism, congestive heart failure, preeclampsia, eclampsia, diabetes mellitus,

hypertension, coronary artery disease, proteinuria, renal insufficiency, or sepsis, type of toxin exposure such as NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, or streptozotocin), clinical variables (e.g., blood pressure, temperature, respiration rate), risk scores (APACHE score, PREDICT score, TIMI Risk Score for UA/NSTEMI, Framingham Risk Score), a glomerular filtration rate, an estimated glomerular filtration rate, a urine production rate, a serum or plasma creatinine concentration, a urine creatinine concentration, a fractional excretion of sodium, a urine sodium concentration, a urine creatinine to serum or plasma creatinine ratio, a urine specific gravity, a urine osmolality, a urine urea nitrogen to plasma urea nitrogen ratio, a plasma BUN to creatnine ratio, a renal failure index calculated as urine sodium / (urine creatinine / plasma creatinine), a serum or plasma neutrophil gelatinase (NGAL) concentration, a urine NGAL concentration, a serum or plasma cystatin C concentration, a serum or plasma cardiac troponin concentration, a serum or plasma BNP concentration, a serum or plasma NTproBNP concentration, and a serum or plasma proBNP concentration. Other measures of renal function which may be combined with one or more kidney injury marker assay result(s) are described hereinafter and in Harrison's Principles of Internal Medicine, 17th Ed., McGraw Hill, New York, pages 1741-1830, and Current Medical Diagnosis & Treatment 2008, 47th Ed, McGraw Hill, New York, pages 785-815, each of which are hereby incorporated by reference in their entirety.

[0043] When more than one marker is measured, the individual markers may be measured in samples obtained at the same time, or may be determined from samples obtained at different (e.g., an earlier or later) times. The individual markers may also be measured on the same or different body fluid samples. For example, one kidney injury marker may be measured in a serum or plasma sample and another kidney injury marker may be measured in a urine sample. In addition, assignment of a likelihood may combine an individual kidney injury marker assay result with temporal changes in one or more additional variables.

[0044] In various related aspects, the present invention also relates to devices and kits for performing the methods described herein. Suitable kits comprise reagents sufficient for performing an assay for at least one of the described kidney injury markers, together with instructions for performing the described threshold comparisons.

[0045] In certain embodiments, reagents for performing such assays are provided in an assay device, and such assay devices may be included in such a kit. Preferred reagents can comprise one or more solid phase antibodies, the solid phase antibody comprising antibody that detects the intended biomarker target(s) bound to a solid support. In the case of sandwich immunoassays, such reagents can also include one or more detectably labeled antibodies, the detectably labeled antibody comprising antibody that detects the intended biomarker target(s) bound to a detectable label. Additional optional elements that may be provided as part of an assay device are described hereinafter.

[0046] Detectable labels may include molecules that are themselves detectable (e.g., fluorescent moieties, electrochemical labels, ecl (electrochemical luminescence) labels, metal chelates, colloidal metal particles, *etc.*) as well as molecules that may be indirectly detected by production of a detectable reaction product (*e.g.*, enzymes such as horseradish peroxidase, alkaline phosphatase, *etc.*) or through the use of a specific binding molecule which itself may be detectable (*e.g.*, a labeled antibody that binds to the second antibody, biotin, digoxigenin, maltose, oligohistidine, 2,4-dintrobenzene, phenylarsenate, ssDNA, dsDNA, *etc.*).

[0047] Generation of a signal from the signal development element can be performed using various optical, acoustical, and electrochemical methods well known in the art. Examples of detection modes include fluorescence, radiochemical detection, reflectance, absorbance, amperometry, conductance, impedance, interferometry, ellipsometry, *etc.* In certain of these methods, the solid phase antibody is coupled to a transducer (*e.g.*, a diffraction grating, electrochemical sensor, etc) for generation of a signal, while in others, a signal is generated by a transducer that is spatially separate from the solid phase antibody (*e.g.*, a fluorometer that employs an excitation light source and an optical detector). This list is not meant to be limiting. Antibody-based biosensors may also be employed to determine the presence or amount of analytes that optionally eliminate the need for a labeled molecule.

[0047A] In one aspect, the present invention provides a kit when used in the method according to the invention, wherein the kit comprises an antibody or antibody fragment that binds specifically to Soluble endothelial protein C receptor.

[0047B] In one aspect, the present invention provides use of Soluble endothelial protein C receptor for one or more of risk stratification, staging, prognosis, classifying and monitoring of the renal status of a subject that is not the recipient of a transplant, and wherein the use comprises assigning a likelihood of one or more future changes in renal status to the subject.

[0047C] In another aspect the present invention provides use of Soluble endothelial protein C receptor for one or more of risk stratification, staging, prognosis, classifying and monitoring of the renal status of a subject suffering from an acute renal injury that is not the recipient of a transplant, and wherein the use comprises assigning a likelihood of one or more future changes in renal status to the subject.

[0047D] In another aspect the present invention provides a method according to the invention, a use of Soluble endothelial protein C receptor according to the invention, or a kit according to the invention, substantially described herein with reference to examples and/or figures.

BRIEF DESCRIPTION OF THE FIGURES

[0046] Fig. 1 provides data tables determined in accordance with Example 6 for the comparison of marker levels in urine samples collected for Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2. Tables provide

descriptive statistics, AUC analysis, and sensitivity, specificity and odds ratio calculations at various threshold (cutoff) levels for the various markers.

[0049] Fig. 2 provides data tables determined in accordance with Example 7 for the comparison of marker levels in urine samples collected for Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2. Tables provide descriptive statistics, AUC analysis, and sensitivity, specificity and odds ratio calculations at various threshold (cutoff) levels for the various markers.

[0050] Fig. 3 provides data tables determined in accordance with Example 8 for the comparison of marker levels in urine samples collected for Cohort 1 (patients that reached, but did not progress beyond, RIFLE stage R) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2. Tables provide descriptive statistics, AUC analysis, and sensitivity, specificity and odds ratio calculations at various threshold (cutoff) levels for the various markers.

[0051] Fig. 4 provides data tables determined in accordance with Example 9 for the comparison of marker levels in urine samples collected for Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2. Tables provide descriptive statistics, AUC analysis, and sensitivity, specificity and odds ratio calculations at various threshold (cutoff) levels for the various markers.

[0052] Fig. 5 provides data tables determined in accordance with Example 6 for the comparison of marker levels in plasma samples collected for Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in plasma samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2. Tables provide descriptive statistics, AUC analysis, and sensitivity, specificity and odds ratio calculations at various threshold (cutoff) levels for the various markers.

[0053] Fig. 6 provides data tables determined in accordance with Example 7 for the comparison of marker levels in plasma samples collected for Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in plasma samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2. Tables provide descriptive statistics, AUC analysis, and sensitivity, specificity and odds ratio calculations at various threshold (cutoff) levels for the various markers.

[0054] Fig. 7 provides data tables determined in accordance with Example 8 for the comparison of marker levels in plasma samples collected for Cohort 1 (patients that reached, but did not progress beyond, RIFLE stage R) and in plasma samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2. Tables provide descriptive statistics, AUC analysis, and sensitivity, specificity and odds ratio calculations at various threshold (cutoff) levels for the various markers.

[0055] Fig. 8 provides data tables determined in accordance with Example 9 for the comparison of marker levels in plasma samples collected for Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in plasma samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2. Tables provide descriptive statistics, AUC analysis, and sensitivity, specificity and odds ratio calculations at various threshold (cutoff) levels for the various markers.

DETAILED DESCRIPTION OF THE INVENTION

[0056] The present invention relates to methods and compositions for diagnosis, differential diagnosis, risk stratification, monitoring, classifying and determination of treatment regimens in subjects suffering or at risk of suffering from injury to renal function, reduced renal function and/or acute renal failure through measurement of one or more kidney injury markers. In various embodiments, a measured concentration of one or more markers selected from the group consisting of Prostatic acid phosphatase, Lactotransferrin, Soluble erythropoietin receptor, Von Willebrand factor, Soluble endothelial protein C receptor, and Beta-2-glycoprotein 1, or one or more markers related thereto, are correlated to the renal status of the subject.

[0057] For purposes of this document, the following definitions apply:

As used herein, an "injury to renal function" is an abrupt (within 14 days, preferably within 7 days, more preferably within 72 hours, and still more preferably within 48 hours) measurable reduction in a measure of renal function. Such an injury may be identified, for example, by a decrease in glomerular filtration rate or estimated GFR, a reduction in urine output, an increase in serum creatinine, an increase in serum cystatin C, a requirement for renal replacement therapy, *etc.* "Improvement in Renal Function" is an abrupt (within 14 days, preferably within 7 days, more preferably within 72 hours, and still more preferably within 48 hours) measurable increase in a measure of renal function. Preferred methods for measuring and/or estimating GFR are described hereinafter.

As used herein, "reduced renal function" is an abrupt (within 14 days, preferably within 7 days, more preferably within 72 hours, and still more preferably within 48 hours) reduction in kidney function identified by an absolute increase in serum creatinine of greater than or equal to 0.1 mg/dL (≥ 8.8 μmol/L), a percentage increase in serum creatinine of greater than or equal to 20% (1.2-fold from baseline), or a reduction in urine output (documented oliguria of less than 0. 5 ml/kg per hour).

As used herein, "acute renal failure" or "ARF" is an abrupt (within 14 days, preferably within 7 days, more preferably within 72 hours, and still more preferably within 48 hours) reduction in kidney function identified by an absolute increase in serum creatinine of greater than or equal to 0.3 mg/dl (≥ 26.4 μmol/l), a percentage increase in serum creatinine of greater than or equal to 50% (1. 5-fold from baseline), or a reduction in urine output (documented oliguria of less than 0.5 ml/kg per hour for at least 6 hours). This term is synonymous with "acute kidney injury" or "AKI."

[0058] In this regard, the skilled artisan will understand that the signals obtained from an immunoassay are a direct result of complexes formed between one or more antibodies and the target biomolecule (*i.e.*, the analyte) and polypeptides containing the necessary epitope(s) to which the antibodies bind. While such assays may detect the full length biomarker and the assay result be expressed as a concentration of a biomarker of interest, the signal from the assay is actually a result of all such "immunoreactive" polypeptides present in the sample. Expression of biomarkers may also be determined by means other than immunoassays, including protein measurements (such as dot blots, western blots, chromatographic methods, mass spectrometry, *etc.*) and nucleic acid measurements (mRNA quatitation). This list is not meant to be limiting.

[0059] As used herein, the term "Prostatic acid phosphatase" refers to one or more polypeptides present in a biological sample that are derived from the Prostatic acid phosphatase precursor (Swiss-Prot P15309 (SEQ ID NO: 1)).

```
        10         20         30         40         50         60
MRAAPLLLAR AASLSLGFLF LLFFWLDRSV LAKELKFVTL VFRHGDRSPI DTFPTDPIKE

        70         80         90        100        110        120
SSWPQGFGQL TQLGMEQHYE LGEYIRKRYR KFLNESYKHE QVYIRSTDVD RTLMSAMTNL

       130        140        150        160        170        180
AALFPPEGVS IWNPILLWQP IPVHTVPLSE DQLLYLPFRN CPRFQELESE TLKSEEFQKR

       190        200        210        220        230        240
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LHPYKDFIAT LGKLSGLHGQ DLFGIWSKVY DPLYCESVHN FTLPSWATED TMTKLRELSE

       250        260        270        280        290        300
LSLLSLYGIH KQKEKSRLQG GVLVNEILNH MKRATQIPSY KKLIMYSAHD TTVSGLQMAL

       310        320        330        340        350        360
DVYNGLLPPY ASCHLTELYF EKGEYFVEMY YRNETQHEPY PLMLPGCSPS CPLERFAELV

       370        380
GPVIPQDWST ECMTTNSHQG TEDSTD
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[0060] The following domains have been identified in Prostatic acid phosphatase:

Residues	Length	Domain ID
1-32	32	Signal sequence
33-386	354	Prostatic acid phosphatase

[0061] As used herein, the term "Lactotransferrin" refers to one or polypeptides present in a biological sample that are derived from the Lactotransferrin precursor (Swiss-Prot P02788 (SEQ ID NO: 2)).

```
        10         20         30         40         50         60
MKLVFLVLLF LGALGLCLAG RRRSVQWCAV SQPEATKCFQ WQRNMRKVRG PPVSCIKRDS

        70         80         90        100        110        120
PIQCIQAIAE NRADAVTLDG GFIYEAGLAP YKLRPVAAEV YGTERQPRTH YYAVAVVKKG

       130        140        150        160        170        180
GSFQLNELQG LKSCHTGLRR TAGWNVPIGT LRPFLNWTGP PEPIEAAVAR FFSASCVPGA

       190        200        210        220        230        240
DKGQFPNLCR LCAGTGENKC AFSSQEPYFS YSGAFKCLRD GAGDVAFIRE STVFEDLSDE

       250        260        270        280        290        300
AERDEYELLC PDNTRKPVDK FKDCHLARVP SHAVVARSVN GKEDAIWNLL RQAQEKFGKD

       310        320        330        340        350        360
KSPKFQLFGS PSGQKDLLFK DSAIGFSRVP PRIDSGLYLG SGYFTAIQNL RKSEEEVAAR

       370        380        390        400        410        420
RARVVWCAVG EQELRKCNQW SGLSEGSVTC SSASTTEDCI ALVLKGEADA MSLDGGYVYT

       430        440        450        460        470        480
AGKCGLVPVL AENYKSQQSS DPDPNCVDRP VEGYLAVAVV RRSDTSLTWN SVKGKKSCHT

       490        500        510        520        530        540
AVDRTAGWNI PMGLLFNQTG SCKFDEYFSQ SCAPGSDPRS NLCALCIGDE QGENKCVPNS

       550        560        570        580        590        600
NERYYGYTGA FRCLAENAGD VAFVKDVTVL QNTDGNNNEA WAKDLKLADF ALLCLDGKRK
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       610         620         630         640         650         660
PVTEARSCHL AMAPNHAVVS RMDKVERLKQ VLLHQQAKFG RNGSDCPDKF CLFQSETKNL

       670         680         690         700         710
LFNDNTECLA RLHGKTTYEK YLGPQYVAGI TNLKKCSTSP LLEACEFLRK
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[0062] Lactotransferrin is cleaved into several smaller polypeptides which include kaliocin-1, lactoferroxin A, lactoferroxin B, and lactoferroxin C. The following domains have been identified in Lactotransferrin:

Residues	Length	Domain ID
1-19	19	Signal sequence
20-710	691	Lactotransferrin
171-201	31	kaliocin-1
338-343	6	lactoferroxin A
543-547	5	lactoferroxin B
680-686	7	lactoferroxin C

[0063] As used herein, the term "Soluble erythropoietin receptor" refers to one or more non-membrane-bound polypeptides present in a biological sample that are derived from the Erythropoietin receptor precursor (Swiss-Prot P19235 (SEQ ID NO: 3)).

```
        10          20          30          40          50          60
MDHLGASLWP QVGSLCLLLA GAAWAPPPNL PDPKFESKAA LLAARGPEEL LCFTERLEDL

        70          80          90         100         110         120
VCFWEEAASA GVGPGNYSFS YQLEDEPWKL CRLHQAPTAR GAVRFWCSLP TADTSSFVPL

       130         140         150         160         170         180
ELRVTAASGA PRYHRVIHIN EVVLLDAPVG LVARLADESG HVVLRWLPPP ETPMTSHIRY

       190         200         210         220         230         240
EVDVSAGNGA GSVQRVEILE GRTECVLSNL RGRTRYTFAV RARMAEPSFG GFWSAWSEPV

       250         260         270         280         290         300
SLLTPSDLDP LILTLSLILV VILVLLTVLA LLSHRRALKQ KIWPGIPSPE SEFEGLFTTH

       310         320         330         340         350         360
KGNFQLWLYQ NDGCLWWSPC TPFTEDPPAS LEVLSERCWG TMQAVEPGTD DEGPLLEPVG

       370         380         390         400         410         420
SEHAQDTYLV LDKWLLPRNP PSEDLPGPGG SVDIVAMDEG SEASSCSSAL ASKPSPEGAS

       430         440         450         460         470         480
```

```
AASFEYTILD PSSQLLRPWT LCPELPPTPP HLKYLYLVVS DSGISTDYSS GDSQGAQGGL

       490        500
SDGPYSNPYE NSLIPAAEPL PPSYVACS
```

or a splice variant thereof (SEQ ID NO: 4)

```
        10         20         30         40         50         60
MDHLGASLWP QVGSLCLLLA GAAWAPPPNL PDPKFESKAA LLAARGPEEL LCFTERLEDL
        70         80         90        100        110        120
VCFWEEAASA GVGPGNYSFS YQLEDEPWKL CRLHQAPTAR GAVRFWCSLP TADTSSFVPL
       130        140        150        160        170        180
ELRVTAASGA PRYHRVIHIN EVVLLDAPVG LVARLADESG HVVLRWLPPP ETPMTSHIRY
       190        200        210        220        230        240
EVDVSAGNGA GSVQRGTVFL SPDWLSSTRA RPHVIYFCLL RVPRPDSAPR WRSWRAAPSV

C
```

(or SEQ ID NO: 5)

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        10         20         30         40         50         60
MDHLGASLWP QVGSLCLLLA GAAWAPPPNL PDPKFESKAA LLAARGPEEL LCFTERLEDL
        70         80         90        100        110        120
VCFWEEAASA GVGPGNYSFS YQLEDEPWKL CRLHQAPTAR GAVRFWCSLP TADTSSFVPL
       130        140        150        160        170        180
ELRVTAASGA PRYHRVIHIN EVVLLDAPVG LVARLADESG HVVLRWLPPP ETPMTSHIRY
       190        200        210        220        230        240
EVDVSAGNGA GSVQRVEILE GRTECVLSNL RGRTRYTFAV RARMAEPSFG GFWSAWSEPV
       250        260        270        280        290        300
SLLTPSDLDP LILTLSLILV VILVLLTVLA LLSHRRALKQ KIWPGIPSPE SEFEGLFTTH
       310        320
KGNFQVGGLV VPSVPGLPCF LQPNCRPL
```

[0064] Erythropoietin receptor is a single-pass type I membrane protein having a large extracellular domain, some or all of which is present in soluble forms of Erythropoietin receptor generated either through alternative splicing event which deletes all or a portion of the transmembrane domain, or by proteolysis of the membrane-bound form. In the case of an immunoassay, one or more antibodies that bind to epitopes within this extracellular domain may be used to detect these soluble form(s). The following domains have been identified in Erythropoietin receptor:

Residues	Length	Domain ID

1-24	24	Signal sequence
25-508	484	Erythropoietin receptor
25-250	226	Extracellular domain
251-273	23	Transmembrane domain
274-508	235	Cytoplasmic domain

[0065] As used herein, the term "Von Willebrand factor" refers to one or polypeptides present in a biological sample that are derived from the Von Willebrand factor precursor (Swiss-Prot P04275 (SEQ ID NO: 6)).

```
        10         20         30         40         50         60
MIPARFAGVL LALALILPGT LCAEGTRGRS STARCSLFGS DFVNTFDGSM YSFAGYCSYL

        70         80         90        100        110        120
LAGGCQKRSF SIIGDFQNGK RVSLSVYLGE FFDIHLFVNG TVTQGDQRVS MPYASKGLYL

       130        140        150        160        170        180
ETEAGYYKLS GEAYGFVARI DGSGNFQVLL SDRYFNKTCG LCGNFNIFAE DDFMTQEGTL

       190        200        210        220        230        240
TSDPYDFANS WALSSGEQWC ERASPPSSSC NISSGEMQKG LWEQCQLLKS TSVFARCHPL

       250        260        270        280        290        300
VDPEPFVALC EKTLCECAGG LECACPALLE YARTCAQEGM VLYGWTDHSA CSPVCPAGME

       310        320        330        340        350        360
YRQCVSPCAR TCQSLHINEM CQERCVDGCS CPEGQLLDEG LCVESTECPC VHSGKRYPPG

       370        380        390        400        410        420
TSLSRDCNTC ICRNSQWICS NEECPGECLV TGQSHFKSFD NRYFTFSGIC QYLLARDCQD

       430        440        450        460        470        480
HSFSIVIETV QCADDRDAVC TRSVTVRLPG LHNSLVKLKH GAGVAMDGQD IQLPLLKGDL

       490        500        510        520        530        540
RIQHTVTASV RLSYGEDLQM DWDGRGRLLV KLSPVYAGKT CGLCGNYNGN QGDDFLTPSG

       550        560        570        580        590        600
LAEPRVEDFG NAWKLHGDCQ DLQKQHSDPC ALNPRMTRFS EEACAVLTSP TFEACHRAVS

       610        620        630        640        650        660
PLPYLRNCRY DVCSCSDGRE CLCGALASYA AACAGRGVRV AWREPGRCEL NCPKGQVYLQ

       670        680        690        700        710        720
CGTPCNLTCR SLSYPDEECN EACLEGCFCP PGLYMDERGD CVPKAQCPCY YDGEIFQPED

       730        740        750        760        770        780
IFSDHHTMCY CEDGFMHCTM SGVPGSLLPD AVLSSPLSHR SKRSLSCRPP MVKLVCPADN
```

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       790        800        810        820        830        840
LRAEGLECTK TCQNYDLECM SMGCVSGCLC PPGMVRHENR CVALERCPCF HQGKEYAPGE

       850        860        870        880        890        900
TVKIGCNTCV CRDRKWNCTD HVCDATCSTI GMAHYLTFDG LKYLFPGECQ YVLVQDYCGS

       910        920        930        940        950        960
NPGTFRILVG NKGCSHPSVK CKKRVTILVE GGEIELFDGE VNVKRPMKDE THFEVVESGR

       970        980        990       1000       1010       1020
YIILLLGKAL SVVWDRHLSI SVVLKQTYQE KVCGLCGNFD GIQNNDLTSS NLQVEEDPVD

      1030       1040       1050       1060       1070       1080
FGNSWKVSSQ CADTRKVPLD SSPATCHNNI MKQTMVDSSC RILTSDVFQD CNKLVDPEPY

      1090       1100       1110       1120       1130       1140
LDVCIYDTCS CESIGDCACF CDTIAAYAHV CAQHGKVVTW RTATLCPQSC EERNLRENGY

      1150       1160       1170       1180       1190       1200
ECEWRYNSCA PACQVTCQHP EPLACPVQCV EGCHAHCPPG KILDELLQTC VDPEDCPVCE

      1210       1220       1230       1240       1250       1260
VAGRRFASGK KVTLNPSDPE HCQICHCDVV NLTCEACQEP GGLVVPPTDA PVSPTTLYVE

      1270       1280       1290       1300       1310       1320
DISEPPLHDF YCSRLLDLVF LLDGSSRLSE AEFEVLKAFV VDMMERLRIS QKWVRVAVVE

      1330       1340       1350       1360       1370       1380
YHDGSHAYIG LKDRKRPSEL RRIASQVKYA GSQVASTSEV LKYTLFQIFS KIDRPEASRI

      1390       1400       1410       1420       1430       1440
ALLLMASQEP QRMSRNFVRY VQGLKKKKVI VIPVGIGPHA NLKQIRLIEK QAPENKAFVL

      1450       1460       1470       1480       1490       1500
SSVDELEQQR DEIVSYLCDL APEAPPPTLP PHMAQVTVGP GLLGVSTLGP KRNSMVLDVA

      1510       1520       1530       1540       1550       1560
FVLEGSDKIG EADFNRSKEF MEEVIQRMDV GQDSIHVTVL QYSYMVTVEY PFSEAQSKGD

      1570       1580       1590       1600       1610       1620
ILQRVREIRY QGGNRTNTGL ALRYLSDHSF LVSQGDREQA PNLVYMVTGN PASDEIKRLP

      1630       1640       1650       1660       1670       1680
GDIQVVPIGV GPNANVQELE RIGWPNAPIL IQDFETLPRE APDLVLQRCC SGEGLQIPTL

      1690       1700       1710       1720       1730       1740
SPAPDCSQPL DVILLLDGSS SFPASYFDEM KSFAKAFISK ANIGPRLTQV SVLQYGSITT

      1750       1760       1770       1780       1790       1800
IDVPWNVVPE KAHLLSLVDV MQREGGPSQI GDALGFAVRY LTSEMHGARP GASKAVVILV

      1810       1820       1830       1840       1850       1860
TDVSVDSVDA AADAARSNRV TVFPIGIGDR YDAAQLRILA GPAGDSNVVK LQRIEDLPTM

      1870       1880       1890       1900       1910       1920
VTLGNSFLHK LCSGFVRICM DEDGNEKRPG DVWTLPDQCH TVTCQPDGQT LLKSHRVNCD
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      1930       1940       1950       1960       1970       1980
RGLRPSCPNS QSPVKVEETC GCRWTCPCVC TGSSTRHIVT FDGQNFKLTG SCSYVLFQNK

      1990       2000       2010       2020       2030       2040
EQDLEVILHN GACSPGARQG CMKSIEVKHS ALSVELHSDM EVTVNGRLVS VPYVGGNMEV

      2050       2060       2070       2080       2090       2100
NVYGAIMHEV RFNHLGHIFT FTPQNNEFQL QLSPKTFASK TYGLCGICDE NGANDFMLRD

      2110       2120       2130       2140       2150       2160
GTVTTDWKTL VQEWTVQRPG QTCQPILEEQ CLVPDSSHCQ VLLLPLFAEC HKVLAPATFY

      2170       2180       2190       2200       2210       2220
AICQQDSCHQ EQVCEVIASY AHLCRTNGVC VDWRTPDFCA MSCPPSLVYN HCEHGCPRHC

      2230       2240       2250       2260       2270       2280
DGNVSSCGDH PSEGCFCPPD KVMLEGSCVP EEACTQCIGE DGVQHQFLEA WVPDHQPCQI

      2290       2300       2310       2320       2330       2340
CTCLSGRKVN CTTQPCPTAK APTCGLCEVA RLRQNADQCC PEYECVCDPV SCDLPPVPHC

      2350       2360       2370       2380       2390       2400
ERGLQPTLTN PGECRPNFTC ACRKEECKRV SPPSCPPHRL PTLRKTQCCD EYECACNCVN

      2410       2420       2430       2440       2450       2460
STVSCPLGYL ASTATNDCGC TTTTCLPDKV CVHRSTIYPV GQFWEEGCDV CTCTDMEDAV

      2470       2480       2490       2500       2510       2520
MGLRVAQCSQ KPCEDSCRSG FTYVLHEGEC CGRCLPSACE VVTGSPRGDS QSSWKSVGSQ

      2530       2540       2550       2560       2570       2580
WASPENPCLI NECVRVKEEV FIQQRNVSCP QLEVPVCPSG FQLSCKTSAC CPSCRCERME

      2590       2600       2610       2620       2630       2640
ACMLNGTVIG PGKTVMIDVC TTCRCMVQVG VISGFKLECR KTTCNPCPLG YKEENNTGEC

      2650       2660       2670       2680       2690       2700
CGRCLPTACT IQLRGGQIMT LKRDETLQDG CDTHFCKVNE RGEYFWEKRV TGCPPFDEHK

      2710       2720       2730       2740       2750       2760
CLAEGGKIMK IPGTCCDTCE EPECNDITAR LQYVKVGSCK SEVEVDIHYC QGKCASKAMY

      2770       2780       2790       2800       2810
SIDINDVQDQ CSCCSPTRTE PMQVALHCTN GSVVYHEVLN AMECKCSPRK CSK
```

[0066] The following domains have been identified in Von Willebrand factor:

Residues	Length	Domain ID
1-24	22	Signal sequence
23-763	227	Von Willebrand antigen 2

764-2813 2050 Von Willebrand factor

[0067] As used herein, the term "Soluble endothelial protein C receptor" refers to one or more non-membrane-bound polypeptides present in a biological sample that are derived from the Erythropoietin receptor precursor (Swiss-Prot Q9UNN8 (SEQ ID NO: 7)).

```
        10         20         30         40         50         60
MLTTLLPILL LSGWAFCSQD ASDGLQRLHM LQISYFRDPY HVWYQGNASL GGHLTHVLEG

        70         80         90        100        110        120
PDTNTTIIQL QPLQEPESWA RTQSGLQSYL LQFHGLVRLV HQERTLAFPL TIRCFLGCEL

       130        140        150        160        170        180
PPEGSRAHVF FEVAVNGSSF VSFRPERALW QADTQVTSGV VTFTLQQLNA YNRTRYELRE

       190        200        210        220        230
FLEDTCVQYV QKHISAENTK GSQTSRSYTS LVLGVLVGSF IIAGVAVGIF LCTGGRRC
```

[0068] Endothelial protein C receptor is a single-pass type I membrane protein having a large extracellular domain, some or all of which is present in soluble forms of Endothelial protein C receptor generated either through alternative splicing event which deletes all or a portion of the transmembrane domain, or by proteolysis of the membrane-bound form. In the case of an immunoassay, one or more antibodies that bind to epitopes within this extracellular domain may be used to detect these soluble form(s). The following domains have been identified in Endothelial protein C receptor:

Residues	Length	Domain ID
1-17	17	Signal sequence
18-238	221	Erythropoietin receptor
18-210	193	Extracellular domain
211-231	21	Transmembrane domain
232-238	7	Cytoplasmic domain

[0069] As used herein, the term "Beta-2-glycoprotein 1" refers to one or polypeptides present in a biological sample that are derived from the Beta-2-glycoprotein 1 precursor (Swiss-Prot P02749 (SEQ ID NO: 8)).

```
        10         20         30         40         50         60
MISPVLILFS SFLCHVAIAG RTCPKPDDLP FSTVVPLKTF YEPGEEITYS CKPGYVSRGG

        70         80         90        100        110        120
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```
MRKFICPLTG LWPINTLKCT PRVCPFAGIL ENGAVRYTTF EYPNTISFSC NTGFYLNGAD

       130        140        150        160        170        180
SAKCTEEGKW SPELPVCAPI ICPPPSIPTF ATLRVYKPSA GNNSLYRDTA VFECLPQHAM

       190        200        210        220        230        240
FGNDTITCTT HGNWTKLPEC REVKCPFPSR PDNGFVNYPA KPTLYYKDKA TFGCHDGYSL

       250        260        270        280        290        300
DGPEEIECTK LGNWSAMPSC KASCKVPVKK ATVVYQGERV KIQEKFKNGM LHGDKVSFFC

       310        320        330        340
KNKEKKCSYT EDAQCIDGTI EVPKCFKEHS SLAFWKTDAS DVKPC
```

[0070] The following domains have been identified in Beta-2-glycoprotein 1:

Residues	Length	Domain ID
1-19	19	Signal sequence
20-345	326	Beta-2-glycoprotein 1

[0071] In addition, several naturally occurring variants have been identified:

Residue	Change
5	V to A
107	S to N
154	R to H
266	V to L
325	C to G
335	W to S

[0072] As used herein, the term "relating a signal to the presence or amount" of an analyte reflects this understanding. Assay signals are typically related to the presence or amount of an analyte through the use of a standard curve calculated using known concentrations of the analyte of interest. As the term is used herein, an assay is "configured to detect" an analyte if an assay can generate a detectable signal indicative of the presence or amount of a physiologically relevant concentration of the analyte. Because an antibody epitope is on the order of 8 amino acids, an immunoassay configured to detect a marker of interest will also detect polypeptides related to the marker sequence, so long as those polypeptides contain the epitope(s) necessary to bind to the antibody or antibodies used in the assay. The term "related marker" as used herein

with regard to a biomarker such as one of the kidney injury markers described herein refers to one or more fragments, variants, etc., of a particular marker or its biosynthetic parent that may be detected as a surrogate for the marker itself or as independent biomarkers. The term also refers to one or more polypeptides present in a biological sample that are derived from the biomarker precursor complexed to additional species, such as binding proteins, receptors, heparin, lipids, sugars, *etc.*

[0073] The term "positive going" marker as that term is used herein refer to a marker that is determined to be elevated in subjects suffering from a disease or condition, relative to subjects not suffering from that disease or condition. The term "negative going" marker as that term is used herein refer to a marker that is determined to be reduced in subjects suffering from a disease or condition, relative to subjects not suffering from that disease or condition.

[0074] The term "subject" as used herein refers to a human or non-human organism. Thus, the methods and compositions described herein are applicable to both human and veterinary disease. Further, while a subject is preferably a living organism, the invention described herein may be used in post-mortem analysis as well. Preferred subjects are humans, and most preferably "patients," which as used herein refers to living humans that are receiving medical care for a disease or condition. This includes persons with no defined illness who are being investigated for signs of pathology.

[0075] Preferably, an analyte is measured in a sample. Such a sample may be obtained from a subject, or may be obtained from biological materials intended to be provided to the subject. For example, a sample may be obtained from a kidney being evaluated for possible transplantation into a subject, and an analyte measurement used to evaluate the kidney for preexisting damage. Preferred samples are body fluid samples.

[0076] The term "body fluid sample" as used herein refers to a sample of bodily fluid obtained for the purpose of diagnosis, prognosis, classification or evaluation of a subject of interest, such as a patient or transplant donor. In certain embodiments, such a sample may be obtained for the purpose of determining the outcome of an ongoing condition or the effect of a treatment regimen on a condition. Preferred body fluid samples include blood, serum, plasma, cerebrospinal fluid, urine, saliva, sputum, and pleural effusions. In addition, one of skill in the art would realize that certain body fluid samples would be

more readily analyzed following a fractionation or purification procedure, for example, separation of whole blood into serum or plasma components.

[0077] The term "diagnosis" as used herein refers to methods by which the skilled artisan can estimate and/or determine the probability ("a likelihood") of whether or not a patient is suffering from a given disease or condition. In the case of the present invention, "diagnosis" includes using the results of an assay, most preferably an immunoassay, for a kidney injury marker of the present invention, optionally together with other clinical characteristics, to arrive at a diagnosis (that is, the occurrence or nonoccurrence) of an acute renal injury or ARF for the subject from which a sample was obtained and assayed. That such a diagnosis is "determined" is not meant to imply that the diagnosis is 100% accurate. Many biomarkers are indicative of multiple conditions. The skilled clinician does not use biomarker results in an informational vacuum, but rather test results are used together with other clinical indicia to arrive at a diagnosis. Thus, a measured biomarker level on one side of a predetermined diagnostic threshold indicates a greater likelihood of the occurrence of disease in the subject relative to a measured level on the other side of the predetermined diagnostic threshold.

[0078] Similarly, a prognostic risk signals a probability ("a likelihood") that a given course or outcome will occur. A level or a change in level of a prognostic indicator, which in turn is associated with an increased probability of morbidity (e.g., worsening renal function, future ARF, or death) is referred to as being "indicative of an increased likelihood" of an adverse outcome in a patient.

[0079] Marker Assays

[0080] In general, immunoassays involve contacting a sample containing or suspected of containing a biomarker of interest with at least one antibody that specifically binds to the biomarker. A signal is then generated indicative of the presence or amount of complexes formed by the binding of polypeptides in the sample to the antibody. The signal is then related to the presence or amount of the biomarker in the sample. Numerous methods and devices are well known to the skilled artisan for the detection and analysis of biomarkers. *See, e.g.*, U.S. Patents 6,143,576; 6,113,855; 6,019,944; 5,985,579; 5,947,124; 5,939,272; 5,922,615; 5,885,527; 5,851,776; 5,824,799; 5,679,526; 5,525,524; and 5,480,792, and *The Immunoassay Handbook*, David Wild, ed. Stockton Press, New

York, 1994, each of which is hereby incorporated by reference in its entirety, including all tables, figures and claims.

[0081] The assay devices and methods known in the art can utilize labeled molecules in various sandwich, competitive, or non-competitive assay formats, to generate a signal that is related to the presence or amount of the biomarker of interest. Suitable assay formats also include chromatographic, mass spectrographic, and protein "blotting" methods. Additionally, certain methods and devices, such as biosensors and optical immunoassays, may be employed to determine the presence or amount of analytes without the need for a labeled molecule. *See, e.g.*, U.S. Patents 5,631,171; and 5,955,377, each of which is hereby incorporated by reference in its entirety, including all tables, figures and claims. One skilled in the art also recognizes that robotic instrumentation including but not limited to Beckman ACCESS®, Abbott AXSYM®, Roche ELECSYS®, Dade Behring STRATUS® systems are among the immunoassay analyzers that are capable of performing immunoassays. But any suitable immunoassay may be utilized, for example, enzyme-linked immunoassays (ELISA), radioimmunoassays (RIAs), competitive binding assays, and the like.

[0082] Antibodies or other polypeptides may be immobilized onto a variety of solid supports for use in assays. Solid phases that may be used to immobilize specific binding members include include those developed and/or used as solid phases in solid phase binding assays. Examples of suitable solid phases include membrane filters, cellulose-based papers, beads (including polymeric, latex and paramagnetic particles), glass, silicon wafers, microparticles, nanoparticles, TentaGels, AgroGels, PEGA gels, SPOCC gels, and multiple-well plates. An assay strip could be prepared by coating the antibody or a plurality of antibodies in an array on solid support. This strip could then be dipped into the test sample and then processed quickly through washes and detection steps to generate a measurable signal, such as a colored spot. Antibodies or other polypeptides may be bound to specific zones of assay devices either by conjugating directly to an assay device surface, or by indirect binding. In an example of the later case, antibodies or other polypeptides may be immobilized on particles or other solid supports, and that solid support immobilized to the device surface.

[0083] Biological assays require methods for detection, and one of the most common methods for quantitation of results is to conjugate a detectable label to a protein or nucleic acid that has affinity for one of the components in the biological system being studied.

Detectable labels may include molecules that are themselves detectable (*e.g.*, fluorescent moieties, electrochemical labels, metal chelates, *etc.*) as well as molecules that may be indirectly detected by production of a detectable reaction product (*e.g.*, enzymes such as horseradish peroxidase, alkaline phosphatase, *etc.*) or by a specific binding molecule which itself may be detectable (e.g., biotin, digoxigenin, maltose, oligohistidine, 2,4-dintrobenzene, phenylarsenate, ssDNA, dsDNA, etc.).

[0084] Preparation of solid phases and detectable label conjugates often comprise the use of chemical cross-linkers. Cross-linking reagents contain at least two reactive groups, and are divided generally into homofunctional cross-linkers (containing identical reactive groups) and heterofunctional cross-linkers (containing non-identical reactive groups). Homobifunctional cross-linkers that couple through amines, sulfhydryls or react non-specifically are available from many commercial sources. Maleimides, alkyl and aryl halides, alpha-haloacyls and pyridyl disulfides are thiol reactive groups. Maleimides, alkyl and aryl halides, and alpha-haloacyls react with sulfhydryls to form thiol ether bonds, while pyridyl disulfides react with sulfhydryls to produce mixed disulfides. The pyridyl disulfide product is cleavable. Imidoesters are also very useful for protein-protein cross-links. A variety of heterobifunctional cross-linkers, each combining different attributes for successful conjugation, are commercially available.

[0085] In certain aspects, the present invention provides kits for the analysis of the described kidney injury markers. The kit comprises reagents for the analysis of at least one test sample which comprise at least one antibody that a kidney injury marker. The kit can also include devices and instructions for performing one or more of the diagnostic and/or prognostic correlations described herein. Preferred kits will comprise an antibody pair for performing a sandwich assay, or a labeled species for performing a competitive assay, for the analyte. Preferably, an antibody pair comprises a first antibody conjugated to a solid phase and a second antibody conjugated to a detectable label, wherein each of the first and second antibodies that bind a kidney injury marker. Most preferably each of the antibodies are monoclonal antibodies. The instructions for use of the kit and performing the correlations can be in the form of labeling, which refers to any written or recorded material that is attached to, or otherwise accompanies a kit at any time during its manufacture, transport, sale or use. For example, the term labeling encompasses advertising leaflets and brochures, packaging materials, instructions, audio or video cassettes, computer discs, as well as writing imprinted directly on kits.

[0086] Antibodies

[0087] The term "antibody" as used herein refers to a peptide or polypeptide derived from, modeled after or substantially encoded by an immunoglobulin gene or immunoglobulin genes, or fragments thereof, capable of specifically binding an antigen or epitope. *See, e.g.* Fundamental Immunology, 3rd Edition, W.E. Paul, ed., Raven Press, N.Y. (1993); Wilson (1994; J. Immunol. Methods 175:267-273; Yarmush (1992) J. Biochem. Biophys. Methods 25:85-97. The term antibody includes antigen-binding portions, i.e., "antigen binding sites," (e.g., fragments, subsequences, complementarity determining regions (CDRs)) that retain capacity to bind antigen, including (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CHl domains; (ii) a F(ab')2 fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CHl domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a dAb fragment (Ward et al., (1989) Nature 341:544-546), which consists of a VH domain; and (vi) an isolated complementarity determining region (CDR). Single chain antibodies are also included by reference in the term "antibody."

[0088] Antibodies used in the immunoassays described herein preferably specifically bind to a kidney injury marker of the present invention. The term "specifically binds" is not intended to indicate that an antibody binds exclusively to its intended target since, as noted above, an antibody binds to any polypeptide displaying the epitope(s) to which the antibody binds. Rather, an antibody "specifically binds" if its affinity for its intended target is about 5-fold greater when compared to its affinity for a non-target molecule which does not display the appropriate epitope(s). Preferably the affinity of the antibody will be at least about 5 fold, preferably 10 fold, more preferably 25-fold, even more preferably 50-fold, and most preferably 100-fold or more, greater for a target molecule than its affinity for a non-target molecule. In preferred embodiments, Preferred antibodies bind with affinities of at least about 10^7 M^{-1}, and preferably between about 10^8 M^{-1} to about 10^9 M^{-1}, about 10^9 M^{-1} to about 10^{10} M^{-1}, or about 10^{10} M^{-1} to about 10^{12} M^{-1} .

[0089] Affinity is calculated as $K_d = k_{off}/k_{on}$ (k_{off} is the dissociation rate constant, K_{on} is the association rate constant and K_d is the equilibrium constant). Affinity can be determined at equilibrium by measuring the fraction bound (r) of labeled ligand at various concentrations (c). The data are graphed using the Scatchard equation: r/c = K(n-r): where r = moles of bound ligand/mole of receptor at equilibrium; c = free ligand concentration

at equilibrium; K = equilibrium association constant; and n = number of ligand binding sites per receptor molecule. By graphical analysis, r/c is plotted on the Y-axis versus r on the X-axis, thus producing a Scatchard plot. Antibody affinity measurement by Scatchard analysis is well known in the art. *See, e.g.*, van Erp *et al., J. Immunoassay* 12: 425-43, 1991; Nelson and Griswold, *Comput. Methods Programs Biomed.* 27: 65-8, 1988.

[0090] The term "epitope" refers to an antigenic determinant capable of specific binding to an antibody. Epitopes usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics. Conformational and nonconformational epitopes are distinguished in that the binding to the former but not the latter is lost in the presence of denaturing solvents.

[0091] Numerous publications discuss the use of phage display technology to produce and screen libraries of polypeptides for binding to a selected analyte. *See, e.g*, Cwirla *et al., Proc. Natl. Acad. Sci. USA* 87, 6378-82, 1990; Devlin *et al., Science* 249, 404-6, 1990, Scott and Smith, *Science* 249, 386-88, 1990; and Ladner *et al.*, U.S. Pat. No. 5,571,698. A basic concept of phage display methods is the establishment of a physical association between DNA encoding a polypeptide to be screened and the polypeptide. This physical association is provided by the phage particle, which displays a polypeptide as part of a capsid enclosing the phage genome which encodes the polypeptide. The establishment of a physical association between polypeptides and their genetic material allows simultaneous mass screening of very large numbers of phage bearing different polypeptides. Phage displaying a polypeptide with affinity to a target bind to the target and these phage are enriched by affinity screening to the target. The identity of polypeptides displayed from these phage can be determined from their respective genomes. Using these methods a polypeptide identified as having a binding affinity for a desired target can then be synthesized in bulk by conventional means. *See, e.g.*, U.S. Patent No. 6,057,098, which is hereby incorporated in its entirety, including all tables, figures, and claims.

[0092] The antibodies that are generated by these methods may then be selected by first screening for affinity and specificity with the purified polypeptide of interest and, if required, comparing the results to the affinity and specificity of the antibodies with polypeptides that are desired to be excluded from binding. The screening procedure can involve immobilization of the purified polypeptides in separate wells of microtiter plates.

The solution containing a potential antibody or groups of antibodies is then placed into the respective microtiter wells and incubated for about 30 min to 2 h. The microtiter wells are then washed and a labeled secondary antibody (for example, an anti-mouse antibody conjugated to alkaline phosphatase if the raised antibodies are mouse antibodies) is added to the wells and incubated for about 30 min and then washed. Substrate is added to the wells and a color reaction will appear where antibody to the immobilized polypeptide(s) are present.

[0093] The antibodies so identified may then be further analyzed for affinity and specificity in the assay design selected. In the development of immunoassays for a target protein, the purified target protein acts as a standard with which to judge the sensitivity and specificity of the immunoassay using the antibodies that have been selected. Because the binding affinity of various antibodies may differ; certain antibody pairs (*e.g.*, in sandwich assays) may interfere with one another sterically, *etc.*, assay performance of an antibody may be a more important measure than absolute affinity and specificity of an antibody.

Assay Correlations

[0094] The term "correlating" as used herein in reference to the use of biomarkers refers to comparing the presence or amount of the biomarker(s) in a patient to its presence or amount in persons known to suffer from, or known to be at risk of, a given condition; or in persons known to be free of a given condition. Often, this takes the form of comparing an assay result in the form of a biomarker concentration to a predetermined threshold selected to be indicative of the occurrence or nonoccurrence of a disease or the likelihood of some future outcome.

[0095] Selecting a diagnostic threshold involves, among other things, consideration of the probability of disease, distribution of true and false diagnoses at different test thresholds, and estimates of the consequences of treatment (or a failure to treat) based on the diagnosis. For example, when considering administering a specific therapy which is highly efficacious and has a low level of risk, few tests are needed because clinicians can accept substantial diagnostic uncertainty. On the other hand, in situations where treatment options are less effective and more risky, clinicians often need a higher degree of diagnostic certainty. Thus, cost/benefit analysis is involved in selecting a diagnostic threshold.

[0096] Suitable thresholds may be determined in a variety of ways. For example, one recommended diagnostic threshold for the diagnosis of acute myocardial infarction using cardiac troponin is the 97.5th percentile of the concentration seen in a normal population. Another method may be to look at serial samples from the same patient, where a prior "baseline" result is used to monitor for temporal changes in a biomarker level.

[0097] Population studies may also be used to select a decision threshold. Reciever Operating Characteristic ("ROC") arose from the field of signal dectection therory developed during World War II for the analysis of radar images, and ROC analysis is often used to select a threshold able to best distinguish a "diseased" subpopulation from a "nondiseased" subpopulation. A false positive in this case occurs when the person tests positive, but actually does not have the disease. A false negative, on the other hand, occurs when the person tests negative, suggesting they are healthy, when they actually do have the disease. To draw a ROC curve, the true positive rate (TPR) and false positive rate (FPR) are determined as the decision threshold is varied continuously. Since TPR is equivalent with sensitivity and FPR is equal to 1 - specificity, the ROC graph is sometimes called the sensitivity vs (1 - specificity) plot. A perfect test will have an area under the ROC curve of 1.0; a random test will have an area of 0.5. A threshold is selected to provide an acceptable level of specificity and sensitivity.

[0098] In this context, "diseased" is meant to refer to a population having one characteristic (the presence of a disease or condition or the occurrence of some outcome) and "nondiseased" is meant to refer to a population lacking the characteristic. While a single decision threshold is the simplest application of such a method, multiple decision thresholds may be used. For example, below a first threshold, the absence of disease may be assigned with relatively high confidence, and above a second threshold the presence of disease may also be assigned with relatively high confidence. Between the two thresholds may be considered indeterminate. This is meant to be exemplary in nature only.

[0099] In addition to threshold comparisons, other methods for correlating assay results to a patient classification (occurrence or nonoccurrence of disease, likelihood of an outcome, *etc.*) include decision trees, rule sets, Bayesian methods, and neural network methods. These methods can produce probability values representing the degree to which a subject belongs to one classification out of a plurality of classifications.

[0100] Measures of test accuracy may be obtained as described in Fischer *et al., Intensive Care Med.* 29: 1043-51, 2003, and used to determine the effectiveness of a given biomarker. These measures include sensitivity and specificity, predictive values, likelihood ratios, diagnostic odds ratios, and ROC curve areas. The area under the curve ("AUC") of a ROC plot is equal to the probability that a classifier will rank a randomly chosen positive instance higher than a randomly chosen negative one. The area under the ROC curve may be thought of as equivalent to the Mann-Whitney U test, which tests for the median difference between scores obtained in the two groups considered if the groups are of continuous data, or to the Wilcoxon test of ranks.

[0101] As discussed above, suitable tests may exhibit one or more of the following results on these various measures: a specificity of greater than 0.5, preferably at least 0.6, more preferably at least 0.7, still more preferably at least 0.8, even more preferably at least 0.9 and most preferably at least 0.95, with a corresponding sensitivity greater than 0.2, preferably greater than 0.3, more preferably greater than 0.4, still more preferably at least 0.5, even more preferably 0.6, yet more preferably greater than 0.7, still more preferably greater than 0.8, more preferably greater than 0.9, and most preferably greater than 0.95; a sensitivity of greater than 0.5, preferably at least 0.6, more preferably at least 0.7, still more preferably at least 0.8, even more preferably at least 0.9 and most preferably at least 0.95, with a corresponding specificity greater than 0.2, preferably greater than 0.3, more preferably greater than 0.4, still more preferably at least 0.5, even more preferably 0.6, yet more preferably greater than 0.7, still more preferably greater than 0.8, more preferably greater than 0.9, and most preferably greater than 0.95; at least 75% sensitivity, combined with at least 75% specificity; a ROC curve area of greater than 0.5, preferably at least 0.6, more preferably 0.7, still more preferably at least 0.8, even more preferably at least 0.9, and most preferably at least 0.95; an odds ratio different from 1, preferably at least about 2 or more or about 0.5 or less, more preferably at least about 3 or more or about 0.33 or less, still more preferably at least about 4 or more or about 0.25 or less, even more preferably at least about 5 or more or about 0.2 or less, and most preferably at least about 10 or more or about 0.1 or less; a positive likelihood ratio (calculated as sensitivity/(1-specificity)) of greater than 1, at least 2, more preferably at least 3, still more preferably at least 5, and most preferably at least 10; and or a negative likelihood ratio (calculated as (1-sensitivity)/specificity) of less than 1, less than or equal

to 0.5, more preferably less than or equal to 0.3, and most preferably less than or equal to 0.1

[0102] Additional clinical indicia may be combined with the kidney injury marker assay result(s) of the present invention. These include other biomarkers related to renal status. Examples include the following, which recite the common biomarker name, followed by the Swiss-Prot entry number for that biomarker or its parent: Actin (P68133); Adenosine deaminase binding protein (DPP4, P27487); Alpha-1-acid glycoprotein 1 (P02763); Alpha-1-microglobulin (P02760); Albumin (P02768); Angiotensinogenase (Renin, P00797); Annexin A2 (P07355); Beta-glucuronidase (P08236); B-2-microglobulin (P61679); Beta-galactosidase (P16278); BMP-7 (P18075); Brain natriuretic peptide (proBNP, BNP-32, NTproBNP; P16860); Calcium-binding protein Beta (S100-beta, P04271); Carbonic anhydrase (Q16790); Casein Kinase 2 (P68400); Cathepsin B (P07858); Ceruloplasmin (P00450); Clusterin (P10909); Complement C3 (P01024); Cysteine-rich protein (CYR61, O00622); Cytochrome C (P99999); Epidermal growth factor (EGF, P01133); Endothelin-1 (P05305); Exosomal Fetuin-A (P02765); Fatty acid-binding protein, heart (FABP3, P05413); Fatty acid-binding protein, liver (P07148); Ferritin (light chain, P02793; heavy chain P02794); Fructose-1,6-biphosphatase (P09467); GRO-alpha (CXCL1, (P09341); Growth Hormone (P01241); Hepatocyte growth factor (P14210); Insulin-like growth factor I (P01343); Immunoglobulin G; Immunoglobulin Light Chains (Kappa and Lambda); Interferon gamma (P01308); Lysozyme (P61626); Interleukin-1alpha (P01583); Interleukin-2 (P60568); Interleukin-4 (P60568); Interleukin-9 (P15248); Interleukin-12p40 (P29460); Interleukin-13 (P35225); Interleukin-16 (Q14005); L1 cell adhesion molecule (P32004); Lactate dehydrogenase (P00338); Leucine Aminopeptidase (P28838); Meprin A-alpha subunit (Q16819); Meprin A-beta subunit (Q16820); Midkine (P21741); MIP2-alpha (CXCL2, P19875); MMP-2 (P08253); MMP-9 (P14780); Netrin-1 (O95631); Neutral endopeptidase (P08473); Osteopontin (P10451); Renal papillary antigen 1 (RPA1); Renal papillary antigen 2 (RPA2); Retinol binding protein (P09455); Ribonuclease; S100 calcium-binding protein A6 (P06703); Serum Amyloid P Component (P02743); Sodium/Hydrogen exchanger isoform (NHE3, P48764); Spermidine/spermine N1-acetyltransferase (P21673); TGF-Beta1 (P01137); Transferrin (P02787); Trefoil factor 3 (TFF3, Q07654); Toll-Like protein 4 (O00206); Total protein; Tubulointerstitial nephritis antigen (Q9UJW2); Uromodulin (Tamm-Horsfall protein, P07911).

[0103] For purposes of risk stratification, Adiponectin (Q15848); Alkaline phosphatase (P05186); Aminopeptidase N (P15144); CalbindinD28k (P05937); Cystatin C (P01034); 8 subunit of F1FO ATPase (P03928); Gamma-glutamyltransferase (P19440); GSTa (alpha-glutathione-S-transferase, P08263); GSTpi (Glutathione-S-transferase P; GST class-pi; P09211); IGFBP-1 (P08833); IGFBP-2 (P18065); IGFBP-6 (P24592); Integral membrane protein 1 (Itm1, P46977); Interleukin-6 (P05231); Interleukin-8 (P10145); Interleukin-18 (Q14116); IP-10 (10 kDa interferon-gamma-induced protein, P02778); IRPR (IFRD1, O00458); Isovaleryl-CoA dehydrogenase (IVD, P26440); I-TAC/CXCL11 (O14625); Keratin 19 (P08727); Kim-1 (Hepatitis A virus cellular receptor 1, O43656); L-arginine:glycine amidinotransferase (P50440); Leptin (P41159); Lipocalin2 (NGAL, P80188); MCP-1 (P13500); MIG (Gamma-interferon-induced monokine Q07325); MIP-1a (P10147); MIP-3a (P78556); MIP-1beta (P13236); MIP-1d (Q16663); NAG (N-acetyl-beta-D-glucosaminidase, P54802); Organic ion transporter (OCT2, O15244); Osteoprotegerin (O14788); P8 protein (O60356); Plasminogen activator inhibitor 1 (PAI-1, P05121); ProANP(1-98) (P01160); Protein phosphatase 1-beta (PPI-beta, P62140); Rab GDI-beta (P50395); Renal kallikrein (Q86U61); RT1.B-1 (alpha) chain of the integral membrane protein (Q5Y7A8); Soluble tumor necrosis factor receptor superfamily member 1A (sTNFR-I, P19438); Soluble tumor necrosis factor receptor superfamily member 1B (sTNFR-II, P20333); Tissue inhibitor of metalloproteinases 3 (TIMP-3, P35625); uPAR (Q03405) may be combined with the kidney injury marker assay result(s) of the present invention.

[0104] Other clinical indicia which may be combined with the kidney injury marker assay result(s) of the present invention includes demographic information (e.g., weight, sex, age, race), medical history (e.g., family history, type of surgery, pre-existing disease such as aneurism, congestive heart failure, preeclampsia, eclampsia, diabetes mellitus, hypertension, coronary artery disease, proteinuria, renal insufficiency, or sepsis, type of toxin exposure such as NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, or streptozotocin), clinical variables (*e.g.*, blood pressure, temperature, respiration rate), risk scores (APACHE score, PREDICT score, TIMI Risk Score for UA/NSTEMI, Framingham Risk Score), a urine total protein measurement, a glomerular filtration rate, an estimated glomerular filtration rate, a urine production rate, a serum or plasma creatinine concentration, a renal papillary antigen 1 (RPA1)

measurement; a renal papillary antigen 2 (RPA2) measurement; a urine creatinine concentration, a fractional excretion of sodium, a urine sodium concentration, a urine creatinine to serum or plasma creatinine ratio, a urine specific gravity, a urine osmolality, a urine urea nitrogen to plasma urea nitrogen ratio, a plasma BUN to creatnine ratio, and/or a renal failure index calculated as urine sodium / (urine creatinine / plasma creatinine). Other measures of renal function which may be combined with the kidney injury marker assay result(s) are described hereinafter and in Harrison's Principles of Internal Medicine, 17th Ed., McGraw Hill, New York, pages 1741-1830, and Current Medical Diagnosis & Treatment 2008, 47th Ed, McGraw Hill, New York, pages 785-815, each of which are hereby incorporated by reference in their entirety.

[0105] Combining assay results/clinical indicia in this manner can comprise the use of multivariate logistical regression, loglinear modeling, neural network analysis, n-of-m analysis, decision tree analysis, etc. This list is not meant to be limiting.

[0106] Diagnosis of Acute Renal Failure

[0107] As noted above, the terms "acute renal (or kidney) injury" and "acute renal (or kidney) failure" as used herein are defined in part in terms of changes in serum creatinine from a baseline value. Most definitions of ARF have common elements, including the use of serum creatinine and, often, urine output. Patients may present with renal dysfunction without an available baseline measure of renal function for use in this comparison. In such an event, one may estimate a baseline serum creatinine value by assuming the patient initially had a normal GFR. Glomerular filtration rate (GFR) is the volume of fluid filtered from the renal (kidney) glomerular capillaries into the Bowman's capsule per unit time. Glomerular filtration rate (GFR) can be calculated by measuring any chemical that has a steady level in the blood, and is freely filtered but neither reabsorbed nor secreted by the kidneys. GFR is typically expressed in units of ml/min:

$$GFR = \frac{\text{Urine Concentration} \times \text{Urine Flow}}{\text{Plasma Concentration}}$$

[0108] By normalizing the GFR to the body surface area, a GFR of approximately 75–100 ml/min per 1.73 m^2 can be assumed. The rate therefore measured is the quantity of the substance in the urine that originated from a calculable volume of blood.

[0109] There are several different techniques used to calculate or estimate the glomerular filtration rate (GFR or eGFR). In clinical practice, however, creatinine clearance is used to measure GFR. Creatinine is produced naturally by the body (creatinine is a metabolite of creatine, which is found in muscle). It is freely filtered by the glomerulus, but also actively secreted by the renal tubules in very small amounts such that creatinine clearance overestimates actual GFR by 10-20%. This margin of error is acceptable considering the ease with which creatinine clearance is measured.

[0110] Creatinine clearance (CCr) can be calculated if values for creatinine's urine concentration (U_{Cr}), urine flow rate (V), and creatinine's plasma concentration (P_{Cr}) are known. Since the product of urine concentration and urine flow rate yields creatinine's excretion rate, creatinine clearance is also said to be its excretion rate ($U_{Cr} \times V$) divided by its plasma concentration. This is commonly represented mathematically as:

$$C_{Cr} = \frac{U_{Cr} \times V}{P_{Cr}}$$

[0111] Commonly a 24 hour urine collection is undertaken, from empty-bladder one morning to the contents of the bladder the following morning, with a comparative blood test then taken:

$$C_{Cr} = \frac{U_{Cr} \times \text{24-hour volume}}{P_{Cr} \times 24 \times 60mins}$$

[0112] To allow comparison of results between people of different sizes, the CCr is often corrected for the body surface area (BSA) and expressed compared to the average sized man as ml/min/1.73 m2. While most adults have a BSA that approaches 1.7 (1.6-1.9), extremely obese or slim patients should have their CCr corrected for their actual BSA:

$$C_{Cr-corrected} = \frac{C_{Cr} \times 1.73}{BSA}$$

[0113] The accuracy of a creatinine clearance measurement (even when collection is complete) is limited because as glomerular filtration rate (GFR) falls creatinine secretion is increased, and thus the rise in serum creatinine is less. Thus, creatinine excretion is much greater than the filtered load, resulting in a potentially large overestimation of the GFR (as much as a twofold difference). However, for clinical purposes it is important to

determine whether renal function is stable or getting worse or better. This is often determined by monitoring serum creatinine alone. Like creatinine clearance, the serum creatinine will not be an accurate reflection of GFR in the non-steady-state condition of ARF. Nonetheless, the degree to which serum creatinine changes from baseline will reflect the change in GFR. Serum creatinine is readily and easily measured and it is specific for renal function.

[0114] For purposes of determining urine output on a Urine output on a mL/kg/hr basis, hourly urine collection and measurement is adequate. In the case where, for example, only a cumulative 24-h output was available and no patient weights are provided, minor modifications of the RIFLE urine output criteria have been described. For example, Bagshaw *et al., Nephrol. Dial. Transplant.* 23: 1203–1210, 2008, assumes an average patient weight of 70 kg, and patients are assigned a RIFLE classification based on the following: <35 mL/h (Risk), <21 mL/h (Injury) or <4 mL/h (Failure).

[0115] Selecting a Treatment Regimen

[0116] Once a diagnosis is obtained, the clinician can readily select a treatment regimen that is compatible with the diagnosis, such as initiating renal replacement therapy, withdrawing delivery of compounds that are known to be damaging to the kidney, kidney transplantation, delaying or avoiding procedures that are known to be damaging to the kidney, modifying diuretic administration, initiating goal directed therapy, *etc.* The skilled artisan is aware of appropriate treatments for numerous diseases discussed in relation to the methods of diagnosis described herein. See, e.g., Merck Manual of Diagnosis and Therapy, 17th Ed. Merck Research Laboratories, Whitehouse Station, NJ, 1999. In addition, since the methods and compositions described herein provide prognostic information, the markers of the present invention may be used to monitor a course of treatment. For example, improved or worsened prognostic state may indicate that a particular treatment is or is not efficacious.

[0117] One skilled in the art readily appreciates that the present invention is well adapted to carry out the embodiments and obtain the ends and advantages mentioned, as well as those inherent therein. The examples provided herein are representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the invention.

[0118] Example 1: Contrast-induced nephropathy sample collection

[0119] The objective of this sample collection study is to collect samples of plasma and urine and clinical data from patients before and after receiving intravascular contrast media. Approximately 250 adults undergoing radiographic/angiographic procedures involving intravascular administration of iodinated contrast media are enrolled. To be enrolled in the study, each patient must meet all of the following inclusion criteria and none of the following exclusion criteria:

Inclusion Criteria

males and females 18 years of age or older;

undergoing a radiographic / angiographic procedure (such as a CT scan or coronary intervention) involving the intravascular administration of contrast media;

expected to be hospitalized for at least 48 hours after contrast administration.

able and willing to provide written informed consent for study participation and to comply with all study procedures.

Exclusion Criteria

renal transplant recipients;

acutely worsening renal function prior to the contrast procedure;

already receiving dialysis (either acute or chronic) or in imminent need of dialysis at enrollment;

expected to undergo a major surgical procedure (such as involving cardiopulmonary bypass) or an additional imaging procedure with contrast media with significant risk for further renal insult within the 48 hrs following contrast administration;

participation in an interventional clinical study with an experimental therapy within the previous 30 days;

known infection with human immunodeficiency virus (HIV) or a hepatitis virus.

[0120] Immediately prior to the first contrast administration (and after any pre-procedure hydration), an EDTA anti-coagulated blood sample (10 mL) and a urine sample (10 mL) are collected from each patient. Blood and urine samples are then collected at 4 (±0.5), 8 (±1), 24 (±2) 48 (±2), and 72 (±2) hrs following the last administration of contrast media during the index contrast procedure. Blood is collected via direct venipuncture or via other available venous access, such as an existing femoral

sheath, central venous line, peripheral intravenous line or hep-lock. These study blood samples are processed to plasma at the clinical site, frozen and shipped to Astute Medical, Inc., San Diego, CA. The study urine samples are frozen and shipped to Astute Medical, Inc.

[0121] Serum creatinine is assessed at the site immediately prior to the first contrast administration (after any pre-procedure hydration) and at 4 (±0.5), 8 (±1), 24 (±2) and 48 (±2)), and 72 (±2) hours following the last administration of contrast (ideally at the same time as the study samples are obtained). In addition, each patient's status is evaluated through day 30 with regard to additional serum and urine creatinine measurements, a need for dialysis, hospitalization status, and adverse clinical outcomes (including mortality).

[0122] Prior to contrast administration, each patient is assigned a risk based on the following assessment: systolic blood pressure <80 mm Hg = 5 points; intra-arterial balloon pump = 5 points; congestive heart failure (Class III-IV or history of pulmonary edema) = 5 points; age >75 yrs = 4 points; hematocrit level <39% for men, <35% for women = 3 points; diabetes = 3 points; contrast media volume = 1 point for each 100 mL; serum creatinine level >1.5 g/dL = 4 points OR estimated GFR 40–60 mL/min/1.73 m^2 = 2 points, 20–40 mL/min/1.73 m^2 = 4 points, < 20 mL/min/1.73 m^2 = 6 points. The risks assigned are as follows: risk for CIN and dialysis: 5 or less total points = risk of CIN - 7.5%, risk of dialysis - 0.04%; 6–10 total points = risk of CIN - 14%, risk of dialysis - 0.12%; 11–16 total points = risk of CIN - 26.1%, risk of dialysis - 1.09%; >16 total points = risk of CIN - 57.3%, risk of dialysis - 12.8%.

[0123] Example 2: Cardiac surgery sample collection

[0124] The objective of this sample collection study is to collect samples of plasma and urine and clinical data from patients before and after undergoing cardiovascular surgery, a procedure known to be potentially damaging to kidney function. Approximately 900 adults undergoing such surgery are enrolled. To be enrolled in the study, each patient must meet all of the following inclusion criteria and none of the following exclusion criteria:

Inclusion Criteria

males and females 18 years of age or older;

undergoing cardiovascular surgery;

Toronto/Ottawa Predictive Risk Index for Renal Replacement risk score of at least 2 (Wijeysundera *et al., JAMA* 297: 1801-9, 2007); and

able and willing to provide written informed consent for study participation and to comply with all study procedures.

Exclusion Criteria

known pregnancy;

previous renal transplantation;

acutely worsening renal function prior to enrollment (e.g., any category of

RIFLE criteria);

already receiving dialysis (either acute or chronic) or in imminent need of dialysis at enrollment;

currently enrolled in another clinical study or expected to be enrolled in another clinical study within 7 days of cardiac surgery that involves drug infusion or a therapeutic intervention for AKI;

known infection with human immunodeficiency virus (HIV) or a hepatitis virus.

[0125] Within 3 hours prior to the first incision (and after any pre-procedure hydration), an EDTA anti-coagulated blood sample (10 mL), whole blood (3 mL), and a urine sample (35 mL) are collected from each patient. Blood and urine samples are then collected at 3 (±0.5), 6 (±0.5), 12 (±1), 24 (±2) and 48 (±2) hrs following the procedure and then daily on days 3 through 7 if the subject remains in the hospital. Blood is collected via direct venipuncture or via other available venous access, such as an existing femoral sheath, central venous line, peripheral intravenous line or hep-lock. These study blood samples are frozen and shipped to Astute Medical, Inc., San Diego, CA. The study urine samples are frozen and shipped to Astute Medical, Inc.

[0126] Example 3: Acutely ill subject sample collection

[0127] The objective of this study is to collect samples from acutely ill patients. Approximately 900 adults expected to be in the ICU for at least 48 hours will be enrolled. To be enrolled in the study, each patient must meet all of the following inclusion criteria and none of the following exclusion criteria:

Inclusion Criteria

males and females 18 years of age or older;

Study population 1: approximately 300 patients that have at least one of:

shock (SBP < 90 mmHg and/or need for vasopressor support to maintain MAP > 60 mmHg and/or documented drop in SBP of at least 40 mmHg); and

sepsis;

Study population 2: approximately 300 patients that have at least one of:

IV antibiotics ordered in computerized physician order entry (CPOE) within 24 hours of enrollment;

contrast media exposure within 24 hours of enrollment;

increased Intra-Abdominal Pressure with acute decompensated heart failure; and

severe trauma as the primary reason for ICU admission and likely to be hospitalized in the ICU for 48 hours after enrollment;

Study population 3: approximately 300 patients

expected to be hospitalized through acute care setting (ICU or ED) with a known risk factor for acute renal injury (*e.g.* sepsis, hypotension/shock (Shock = systolic BP < 90 mmHg and/or the need for vasopressor support to maintain a MAP > 60 mmHg and/or a documented drop in SBP > 40 mmHg), major trauma, hemorrhage, or major surgery); and/or expected to be hospitalized to the ICU for at least 24 hours after enrollment.

Exclusion Criteria

known pregnancy;

institutionalized individuals;

previous renal transplantation;

known acutely worsening renal function prior to enrollment (e.g., any category of RIFLE criteria);

received dialysis (either acute or chronic) within 5 days prior to enrollment or in imminent need of dialysis at the time of enrollment;

known infection with human immunodeficiency virus (HIV) or a hepatitis virus;

meets only the SBP < 90 mmHg inclusion criterion set forth above, and does not have shock in the attending physician's or principal investigator's opinion.

[0128] After providing informed consent, an EDTA anti-coagulated blood sample (10 mL) and a urine sample (25-30 mL) are collected from each patient. Blood and urine samples are then collected at 4 (± 0.5) and 8 (± 1) hours after contrast administration (if applicable); at 12 (± 1), 24 (± 2), and 48 (± 2) hours after enrollment, and thereafter daily up to day 7 to day 14 while the subject is hospitalized. Blood is collected via direct venipuncture or via other available venous access, such as an existing femoral sheath, central venous line, peripheral intravenous line or hep-lock. These study blood samples are processed to plasma at the clinical site, frozen and shipped to Astute Medical, Inc., San Diego, CA. The study urine samples are frozen and shipped to Astute Medical, Inc.

[0129] Example 4. Immunoassay format

[0130] Analytes are is measured using standard sandwich enzyme immunoassay techniques. A first antibody which binds the analyte is immobilized in wells of a 96 well polystyrene microplate. Analyte standards and test samples are pipetted into the appropriate wells and any analyte present is bound by the immobilized antibody. After washing away any unbound substances, a horseradish peroxidase-conjugated second antibody which binds the analyte is added to the wells, thereby forming sandwich complexes with the analyte (if present) and the first antibody. Following a wash to remove any unbound antibody-enzyme reagent, a substrate solution comprising tetramethylbenzidine and hydrogen peroxide is added to the wells. Color develops in proportion to the amount of analyte present in the sample. The color development is stopped and the intensity of the color is measured at 540 nm or 570 nm. An analyte concentration is assigned to the test sample by comparison to a standard curve determined from the analyte standards.

[0131] Concentrations are expressed in the following examples as follows: Prostatic acid phosphatase – ng/mL, Lactotransferrin – ng/mL, Soluble erythropoietin receptor – pg/mL, Von Willebrand factor – μg/mL, Soluble endothelial protein C receptor – pg/mL, and Beta-2-glycoprotein 1 – pg/mL.

[0132] Example 5. Apparently Healthy Donor and Chronic Disease Patient Samples

[0133] Human urine samples from donors with no known chronic or acute disease ("Apparently Healthy Donors") were purchased from two vendors (Golden West Biologicals, Inc., 27625 Commerce Center Dr., Temecula, CA 92590 and Virginia Medical Research, Inc., 915 First Colonial Rd., Virginia Beach, VA 23454). The urine samples were shipped and stored frozen at less than -20° C. The vendors supplied demographic information for the individual donors including gender, race (Black /White), smoking status and age.

[0134] Human urine samples from donors with various chronic diseases ("Chronic Disease Patients") including congestive heart failure, coronary artery disease, chronic kidney disease, chronic obstructive pulmonary disease, diabetes mellitus and hypertension were purchased from Virginia Medical Research, Inc., 915 First Colonial Rd., Virginia Beach, VA 23454. The urine samples were shipped and stored frozen at less than -20 degrees centigrade. The vendor provided a case report form for each individual donor with age, gender, race (Black/White), smoking status and alcohol use, height, weight, chronic disease(s) diagnosis, current medications and previous surgeries.

[0135] Example 6. Kidney injury markers for evaluating renal status in patients at RIFLE Stage 0

[0136] Patients from the intensive care unit (ICU) were classified by kidney status as non-injury (0), risk of injury (R), injury (I), and failure (F) according to the maximum stage reached within 7 days of enrollment as determined by the RIFLE criteria.

[0137] Two cohorts were defined as (Cohort 1) patients that did not progress beyond stage 0, and (Cohort 2) patients that reached stage R, I, or F within 10 days. To address normal marker fluctuations that occur within patients at the ICU and thereby assess utility for monitoring AKI status, marker levels were measured in urine samples collected for Cohort 1. Marker concentrations were measured in urine samples collected from a subject at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2. In the following tables, the time "prior max stage" represents the time at which a sample is collected, relative to the time a particular patient reaches the lowest disease stage as defined for that cohort, binned into three groups which are +/- 12 hours. For example, 24 hr prior for this example (0 vs R, I, F) would mean 24 hr (+/- 12 hours) prior to reaching stage R (or I if no sample at R, or F if no sample at R or I).

[0138] Each marker was measured by standard immunoassay methods using commercially available assay reagents. A receiver operating characteristic (ROC) curve was generated for each marker and the area under each ROC curve (AUC) was determined. Patients in Cohort 2 were also separated according to the reason for adjudication to stage R, I, or F as being based on serum creatinine measurements (sCr), being based on urine output (UO), or being based on either serum creatinine measurements or urine output. That is, for those patients adjudicated to stage R, I, or F on the basis of serum creatinine measurements alone, the stage 0 cohort may have included patients adjudicated to stage R, I, or F on the basis of urine output; for those patients adjudicated to stage R, I, or F on the basis of urine output alone, the stage 0 cohort may have included patients adjudicated to stage R, I, or F on the basis of serum creatinine measurements; and for those patients adjudicated to stage R, I, or F on the basis of serum creatinine measurements or urine output, the stage 0 cohort contains only patients in stage 0 for both serum creatinine measurements and urine output. Also, for those patients adjudicated to stage R, I, or F on the basis of serum creatinine measurements or urine output, the adjudication method which yielded the most severe RIFLE stage was used.

[0139] The ability to distinguish cohort 1 (subjects remaining in RIFLE 0) from Cohort 2 (subjects progressing to RIFLE R, I or F) was determined using ROC analysis. SE is the standard error of the AUC, n is the number of sample or individual patients ("pts," as indicated). Standard errors were calculated as described in Hanley, J. A., and McNeil, B.J., The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology (1982) 143: 29-36; p values were calculated with a two-tailed Z-test. An AUC < 0.5 is indicative of a negative going marker for the comparison, and an AUC > 0.5 is indicative of a positive going marker for the comparison.

[0140] Various threshold (or "cutoff") concentrations were selected, and the associated sensitivity and specificity for distinguishing cohort 1 from cohort 2 were determined. OR is the odds ratio calculated for the particular cutoff concentration, and 95% CI is the confidence interval for the odds ratio.

[0141] The results of these three analyses for various markers of the present invention are presented in Fig. 1.

[0142] Example 7. Kidney injury markers for evaluating renal status in patients at RIFLE Stages 0 and R

[0143] Patients were classified and analyzed as described in Example 6. However, patients that reached stage R but did not progress to stage I or F were grouped with patients from non-injury stage 0 in Cohort 1. Cohort 2 in this example included only patients that progressed to stage I or F. Marker concentrations in urine samples were included for Cohort 1. Marker concentrations in urine samples collected within 0, 24, and 48 hours of reaching stage I or F were included for Cohort 2.

[0144] The ability to distinguish cohort 1 (subjects remaining in RIFLE 0 or R) from Cohort 2 (subjects progressing to RIFLE I or F) was determined using ROC analysis.

[0145] Various threshold (or "cutoff") concentrations were selected, and the associated sensitivity and specificity for distinguishing cohort 1 from cohort 2 were determined. OR is the odds ratio calculated for the particular cutoff concentration, and 95% CI is the confidence interval for the odds ratio.

[0146] The results of these three analyses for various markers of the present invention are presented in Fig. 2.

[0147] Example 8. Kidney injury markers for evaluating renal status in patients progressing from Stage R to Stages I and F

[0148] Patients were classified and analyzed as described in Example 6, but only those patients that reached Stage R were included in this example. Cohort 1 contained patients that reached stage R but did not progress to stage I or F within 10 days, and Cohort 2 included only patients that progressed to stage I or F. Marker concentrations in urine samples collected within 12 hours of reaching stage R were included in the analysis for both Cohort 1 and 2.

[0149] The ability to distinguish cohort 1 (subjects remaining in RIFLE R) from Cohort 2 (subjects progressing to RIFLE I or F) was determined using ROC analysis.

[0150] Various threshold (or "cutoff") concentrations were selected, and the associated sensitivity and specificity for distinguishing cohort 1 from cohort 2 were determined. OR is the odds ratio calculated for the particular cutoff concentration, and 95% CI is the confidence interval for the odds ratio.

[0151] The results of these three analyses for various markers of the present invention are presented in Fig. 3.

[0152] Example 9. Kidney injury markers for evaluating renal status in patients at RIFLE Stage 0

[0153] Patients were classified and analyzed as described in Example 6. However, patients that reached stage R or I but did not progress to stage F were eliminated from the analysis. Patients from non-injury stage 0 are included in Cohort 1. Cohort 2 in this example included only patients that progressed to stage F. The maximum marker concentrations in urine samples were included for each patient in Cohort 1. The maximum marker concentrations in urine samples collected within 0, 24, and 48 hours of reaching stage F were included for each patient in Cohort 2.

[0154] The ability to distinguish cohort 1 (subjects remaining in RIFLE 0 or R) from Cohort 2 (subjects progressing to RIFLE I or F) was determined using ROC analysis.

[0155] Various threshold (or "cutoff") concentrations were selected, and the associated sensitivity and specificity for distinguishing cohort 1 from cohort 2 were determined. OR is the odds ratio calculated for the particular cutoff concentration, and 95% CI is the confidence interval for the odds ratio.

[0156] The results of these three analyses for various markers of the present invention are presented in Fig. 4.

[0157] Example 10. Kidney injury markers for evaluating renal status in patients at RIFLE Stage 0

[0158] Patients from the intensive care unit (ICU) were classified by kidney status as non-injury (0), risk of injury (R), injury (I), and failure (F) according to the maximum stage reached within 7 days of enrollment as determined by the RIFLE criteria.

[0159] Two cohorts were defined as (Cohort 1) patients that did not progress beyond stage 0, and (Cohort 2) patients that reached stage R, I, or F within 10 days. To address normal marker fluctuations that occur within patients at the ICU and thereby assess utility for monitoring AKI status, marker levels were measured in the plasma component of blood samples collected for Cohort 1. Marker concentrations were measured in the plasma component of blood samples collected from a subject at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2. In the following tables, the time "prior max stage" represents the time at which a sample is collected, relative to the time a particular patient reaches the lowest disease stage as defined for that cohort, binned into three groups which are +/- 12 hours. For example, 24 hr prior for this example (0 vs R, I, F)

would mean 24 hr (+/- 12 hours) prior to reaching stage R (or I if no sample at R, or F if no sample at R or I).

[0160] Each marker was measured by standard immunoassay methods using commercially available assay reagents. A receiver operating characteristic (ROC) curve was generated for each marker and the area under each ROC curve (AUC) was determined. Patients in Cohort 2 were also separated according to the reason for adjudication to stage R, I, or F as being based on serum creatinine measurements (sCr), being based on urine output (UO), or being based on either serum creatinine measurements or urine output. That is, for those patients adjudicated to stage R, I, or F on the basis of serum creatinine measurements alone, the stage 0 cohort may have included patients adjudicated to stage R, I, or F on the basis of urine output; for those patients adjudicated to stage R, I, or F on the basis of urine output alone, the stage 0 cohort may have included patients adjudicated to stage R, I, or F on the basis of serum creatinine measurements; and for those patients adjudicated to stage R, I, or F on the basis of serum creatinine measurements or urine output, the stage 0 cohort contains only patients in stage 0 for both serum creatinine measurements and urine output. Also, for those patients adjudicated to stage R, I, or F on the basis of serum creatinine measurements or urine output, the adjudication method which yielded the most severe RIFLE stage was used.

[0161] The ability to distinguish cohort 1 (subjects remaining in RIFLE 0) from Cohort 2 (subjects progressing to RIFLE R, I or F) was determined using ROC analysis. SE is the standard error of the AUC, n is the number of sample or individual patients ("pts," as indicated). Standard errors were calculated as described in Hanley, J. A., and McNeil, B.J., The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology (1982) 143: 29-36; p values were calculated with a two-tailed Z-test. An AUC < 0.5 is indicative of a negative going marker for the comparison, and an AUC > 0.5 is indicative of a positive going marker for the comparison.

[0162] Various threshold (or "cutoff") concentrations were selected, and the associated sensitivity and specificity for distinguishing cohort 1 from cohort 2 were determined. OR is the odds ratio calculated for the particular cutoff concentration, and 95% CI is the confidence interval for the odds ratio.

[0163] The results of these three analyses for various markers of the present invention are presented in Fig. 5.

[0164] Example 11. Kidney injury markers for evaluating renal status in patients at RIFLE Stages 0 and R

[0165] Patients were classified and analyzed as described in Example 10. However, patients that reached stage R but did not progress to stage I or F were grouped with patients from non-injury stage 0 in Cohort 1. Cohort 2 in this example included only patients that progressed to stage I or F. Marker concentrations in the plasma component of blood samples were included for Cohort 1. Marker concentrations in the plasma component of blood samples collected within 0, 24, and 48 hours of reaching stage I or F were included for Cohort 2.

[0166] The ability to distinguish cohort 1 (subjects remaining in RIFLE 0 or R) from Cohort 2 (subjects progressing to RIFLE I or F) was determined using ROC analysis.

[0167] Various threshold (or "cutoff") concentrations were selected, and the associated sensitivity and specificity for distinguishing cohort 1 from cohort 2 were determined. OR is the odds ratio calculated for the particular cutoff concentration, and 95% CI is the confidence interval for the odds ratio.

[0168] The results of these three analyses for various markers of the present invention are presented in Fig. 6.

[0169] Example 12. Kidney injury markers for evaluating renal status in patients progressing from Stage R to Stages I and F

[0170] Patients were classified and analyzed as described in Example 10, but only those patients that reached Stage R were included in this example. Cohort 1 contained patients that reached stage R but did not progress to stage I or F within 10 days, and Cohort 2 included only patients that progressed to stage I or F. Marker concentrations in the plasma component of blood samples collected within 12 hours of reaching stage R were included in the analysis for both Cohort 1 and 2.

[0171] The ability to distinguish cohort 1 (subjects remaining in RIFLE R) from Cohort 2 (subjects progressing to RIFLE I or F) was determined using ROC analysis.

[0172] Various threshold (or "cutoff") concentrations were selected, and the associated sensitivity and specificity for distinguishing cohort 1 from cohort 2 were determined. OR is the odds ratio calculated for the particular cutoff concentration, and 95% CI is the confidence interval for the odds ratio.

[0173] The results of these three analyses for various markers of the present invention are presented in Fig. 7.

[0174] Example 13. Kidney injury markers for evaluating renal status in patients at RIFLE Stage 0

[0175] Patients were classified and analyzed as described in Example 10. However, patients that reached stage R or I but did not progress to stage F were eliminated from the analysis. Patients from non-injury stage 0 are included in Cohort 1. Cohort 2 in this example included only patients that progressed to stage F. The maximum marker concentrations in the plasma component of blood samples were included from each patient in Cohort 1. The maximum marker concentrations in the plasma component of blood samples collected within 0, 24, and 48 hours of reaching stage F were included from each patient in Cohort 2.

[0176] The ability to distinguish cohort 1 (subjects remaining in RIFLE 0 or R) from Cohort 2 (subjects progressing to RIFLE I or F) was determined using ROC analysis.

[0177] Various threshold (or "cutoff") concentrations were selected, and the associated sensitivity and specificity for distinguishing cohort 1 from cohort 2 were determined. OR is the odds ratio calculated for the particular cutoff concentration, and 95% CI is the confidence interval for the odds ratio.

[0178] The results of these three analyses for various markers of the present invention are presented in Fig. 8.

[0179] While the invention has been described and exemplified in sufficient detail for those skilled in this art to make and use it, various alternatives, modifications, and improvements should be apparent without departing from the spirit and scope of the invention. The examples provided herein are representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the invention. Modifications therein and other uses will occur to those skilled in the art. These modifications are encompassed within the spirit of the invention and are defined by the scope of the claims.

[0180] It will be readily apparent to a person skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention.

[0181] All patents and publications mentioned in the specification are indicative of the levels of those of ordinary skill in the art to which the invention pertains. All patents and publications are herein incorporated by reference to the same extent as if each individual publication was specifically and individually indicated to be incorporated by reference.

[0182] The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments and optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the appended claims.

[0183] Other embodiments are set forth within the following claims.

We claim:

1. A method for evaluating renal status in a subject that is not the recipient of a transplant, comprising:

performing one or more assays configured to detect one or more kidney injury marker(s) in a body fluid sample obtained from the subject to provide an assay result(s), wherein at least one of said markers is Soluble endothelial protein C receptor;

determining an assay result(s) for each assay comprising a measured concentration of one or more kidney injury marker(s); and

correlating the assay result(s) to one or more of risk stratification, staging, prognosis, classifying and monitoring of the renal status of the subject,

wherein said correlating step comprises assigning a likelihood of one or more future changes in renal status to the subject based on the assay result(s).

2. A method of claim 1, wherein said one or more future changes in renal status comprise one or more of a future injury to renal function, future reduced renal function, future improvement in renal function, and future acute renal failure (ARF).

3. A method according to claim 1 or claim 2, further comprising one or more assays to detect as least one or more of:

(i) a measured concentration of Prostatic acid phosphatase,

(ii) a measured concentration of Lactotransferrin,

(iii) a measured concentration of Soluble erythropoietin receptor,

(iv) a measured concentration of Von Willebrand factor,

(v) a measured concentration of Beta-2-glycoprotein 1,

and said correlation step comprises, for each assay result, comparing said measured concentration to a threshold concentration, and

for a positive going marker, assigning an increased likelihood of suffering a future injury to renal function, future reduced renal function, future ARF, or a future improvement in renal function to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold or assigning a decreased likelihood of suffering a future injury to renal function, future reduced renal function, future ARF, or a future improvement in renal function to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold, or

for a negative going marker, assigning an increased likelihood of suffering a future injury to renal function, future reduced renal function, future ARF, or a future improvement in renal function to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold or assigning a decreased likelihood of suffering a future injury to renal function, future reduced renal function, future ARF, or a future improvement in renal function to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold.

4. A method according to any one of claims 1 to 3, wherein said one or more future changes in renal status comprise a clinical outcome related to a renal injury suffered by the subject.

5. A method according to any one of claims 1 to 4, further comprising one or more assays to detect at least one or more of:

(i) a measured concentration of Prostatic acid phosphatase,

(ii) a measured concentration of Lactotransferrin,

(iii) a measured concentration of Soluble erythropoietin receptor,

(iv) a measured concentration of Von Willebrand factor,

(v) a measured concentration of Beta-2-glycoprotein 1,

and said correlation step comprises, for each assay result, comparing said measured concentration to a threshold concentration, and

for a positive going marker, assigning an increased likelihood of subsequent acute kidney injury, worsening stage of AKI, mortality, need for renal replacement therapy, need for withdrawal of renal toxins, end stage renal disease, heart failure, stroke, myocardial infarction, or chronic kidney disease to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold, or assigning a decreased likelihood of subsequent acute kidney injury, worsening stage of AKI, mortality, need for renal replacement therapy, need for withdrawal of renal toxins, end stage renal disease, heart failure, stroke, myocardial infarction, or chronic kidney disease to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold, or

for a negative going marker, assigning an increased likelihood of subsequent acute kidney injury, worsening stage of AKI, mortality, need for renal replacement therapy, need for withdrawal of renal toxins, end stage renal disease, heart failure, stroke, myocardial infarction, or chronic kidney disease to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold, or assigning a decreased likelihood of subsequent acute kidney injury, worsening stage of AKI, mortality, need for renal replacement therapy, need for withdrawal of renal toxins, end stage renal disease, heart failure, stroke, myocardial infarction, or chronic kidney disease to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold.

6. A method according to any one of claims 1 to 5, wherein the likelihood of one or more future changes in renal status is that an event of interest is more or less likely to occur within a period selected from the group consisting of 30 days, 21 days, 14 days, 7 days, 5 days, 96 hours, 72 hours, 48 hours, 36 hours, 24 hours, and 12 hours.

7. A method according to any one of claims 1 to 6, wherein the subject is selected for evaluation of renal status based on the pre-existence in the subject of one or more known risk factors for prerenal, intrinsic renal, or postrenal ARF.

8. A method according to any one of claims 1 to 7, wherein the subject is selected for evaluation of renal status based on an existing diagnosis of one or more of congestive heart failure, preeclampsia, eclampsia, diabetes mellitus, hypertension, coronary artery disease, proteinuria, renal insufficiency, glomerular filtration below the normal range, cirrhosis, serum creatinine above the normal range, sepsis, injury to renal function, reduced renal function, or ARF, or based on undergoing or having undergone major vascular surgery, coronary artery bypass, or other cardiac surgery, or based on exposure to NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, or streptozotocin.

9. A method according to any one of claims 1 to 8, wherein said correlating step further comprises assigning a diagnosis of the occurrence or nonoccurrence of one or more of an injury to renal function, reduced renal function, or ARF to the subject based on the assay result(s).

10. A method according to claim 1, wherein said correlating step further comprises assessing whether or not renal function is improving or worsening in a subject who has suffered from an injury to renal function, reduced renal function, or ARF based on the assay result(s).

11. A method according to claim 10, further comprising one or more assays to detect at least one or more of:

(i) a measured concentration of Prostatic acid phosphatase,

(ii) a measured concentration of Lactotransferrin,

(iii) a measured concentration of Soluble erythropoietin receptor,

(iv) a measured concentration of Von Willebrand factor,

(v) a measured concentration of Beta-2-glycoprotein 1,

and said correlation step comprises, for each assay result, comparing said measured concentration to a threshold concentration, and

for a positive going marker, assigning a worsening of renal function to the subject when the measured concentration is above the threshold, or assigning an improvement of renal function when the measured concentration is below the threshold, or

for a negative going marker, assigning a worsening of renal function to the subject when the measured concentration is below the threshold, or assigning an improvement of renal function when the measured concentration is above the threshold.

12. A method according to claim 1, wherein said method is a method of assigning a risk of the future occurrence or nonoccurrence in a subject of one or more of:

i) an injury to renal function;

ii) reduced renal function in;

iii) acute renal failure;

iv) a need for renal replacement therapy; and

v) a need for renal transplantation.

13. A method according to claim 3, wherein said one or more future changes in renal status comprise one or more of a future injury to renal function, future reduced renal function, future improvement in renal function, and future acute renal failure (ARF) within 72 hours, 48 hours, or 24 hours of the time at which the body fluid sample was obtained.

14. A method according to claim 5, wherein the increased or decreased likelihood of subsequent acute kidney injury, worsening stage of AKI, mortality, need for renal replacement therapy, need for withdrawal of renal toxins, end stage renal disease, heart failure, stroke, myocardial infarction, or chronic kidney disease assigned to the subject is a likelihood that an event of interest is more or less likely to occur within 30 days, or 72 hours or 24 hours of the time at which the body fluid sample was obtained from the subject.

15. A method according to any one of claim 1 to 14, wherein the body fluid comprises urine, blood, serum or plasma.

16. Use of Soluble endothelial protein C receptor when used for one or more of risk stratification, staging, prognosis, classifying and monitoring of the renal status of a subject that is not the recipient of a transplant, and

wherein the use comprises assigning a likelihood of one or more future changes in renal status to the subject.

17. Use of Soluble endothelial protein C receptor when used one or more of risk stratification, staging, prognosis, classifying and monitoring of the renal status of a subject suffering from an acute renal injury that is not the recipient of a transplant, and

wherein the use comprises assigning a likelihood of one or more future changes in renal status to the subject.

18. A kit when used in the method according to any one of claims 1 to 15, wherein the kit comprises an antibody or antibody fragment that binds specifically to Soluble endothelial protein C receptor.

19. A method according to any one of claims 1 to 15, the use of Soluble endothelial protein C receptor according to claim 16 or claim 17 or the kit according to claim 18, substantially described herein with reference to examples and/or figures.

Endothelial protein C receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	43.929	60.385	43.929	61.154	43.929	0.962
average	68.904	77.746	68.904	82.203	68.904	80.385
stdev	83.580	71.173	83.580	54.662	83.580	na
p (t-test)		0.672		0.504		na
min	0.962	2.885	0.962	0.068	0.962	80.385
max	491.892	266.981	491.892	187.645	491.892	80.385
n (Samp)	51	21	51	21	51	1
n (Pat)	40	21	40	21	40	1

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	54.309	20.808	54.309	58.077	54.309	50.484
average	76.435	27.244	76.435	72.976	76.435	50.484
stdev	73.686	26.662	73.686	57.184	73.686	30.484
p (t-test)		0.108		0.904		0.622
min	0.962	2.885	0.962	0.068	0.962	28.929
max	491.892	79.276	491.892	153.737	491.892	72.039
n (Samp)	92	6	92	7	92	2
n (Pat)	73	6	73	7	73	2

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	43.522	76.974	43.522	63.158	43.522	58.031
average	69.978	93.411	69.978	95.567	69.978	49.833
stdev	88.824	73.608	88.824	64.336	88.824	37.304
p (t-test)		0.352		0.275		0.658
min	11.218	21.189	11.218	23.476	11.218	2.885
max	491.892	266.981	491.892	258.333	491.892	80.385
n (Samp)	42	16	42	18	42	4
n (Pat)	33	16	33	18	33	4

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.56	0.076	51	21	0.431
24 hours	0.63	0.075	51	21	0.077
48 hours	0.80	0.268	51	1	0.257

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.19	0.070	92	6	0.000
24 hours	0.51	0.114	92	7	0.946
48 hours	0.43	0.195	92	2	0.718

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.67	0.084	42	16	0.048
24 hours	0.70	0.078	42	18	0.009
48 hours	0.51	0.153	42	4	0.969

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	27.898551	71%	29%	1			
	20.833333	86%	20%	2	0.7	0.2	2.4
	19.664634	90%	18%	3	0.7	0.2	2.4
	62.828947	48%	71%	4	2.1	0.8	5.6
	75	43%	80%				
	174.51737	10%	90%				

FIG. 1 - 1

24 hours	47.463768	71%	53%	1			
	38.928571	81%	45%	2	0.7	0.2	2.9
	22.115385	90%	25%	3	1.3	0.4	4.3
	62.828947	43%	71%	4	3.5	1.2	10.2
	75	43%	80%				
	174.51737	5%	90%				
48 hours	75	100%	80%	1			
	75	100%	80%	2	na	na	na
	75	100%	80%	3	na	na	na
	62.828947	100%	71%	4	na	na	na
	75	100%	80%				
	174.51737	0%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	13.782051	83%	4%	1			
	13.782051	83%	4%	2	na	na	na
	0.9615385	100%	1%	3	na	na	na
	81.923077	0%	71%	4	na	na	na
	111.74377	0%	80%				
	161.38996	0%	90%				
24 hours	55	71%	51%	1			
	11.217949	86%	3%	2	0.0	0.0	na
	0	100%	0%	3	1.0	0.1	8.1
	81.923077	43%	71%	4	1.5	0.2	9.2
	111.74377	29%	80%				
	161.38996	0%	90%				
48 hours	28.623188	100%	23%	1			
	28.623188	100%	23%	2	na	na	na
	28.623188	100%	23%	3	na	na	na
	81.923077	0%	71%	4	na	na	na
	111.74377	0%	80%				
	161.38996	0%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	32.246377	75%	38%	1			
	30.072464	81%	36%	2	6.5	0.4	96.6
	26.449275	94%	33%	3	3.5	0.2	67.2
	59.539474	63%	71%	4	11.4	0.8	158.7
	75	50%	81%				
	153.73665	13%	90%				
24 hours	53.618421	72%	62%	1			
	43.928571	83%	52%	2	1.6	0.2	11.4
	24.038462	94%	31%	3	3.3	0.6	18.1
	59.539474	61%	71%	4	7.4	1.4	38.9
	75	44%	81%				
	153.73665	22%	90%				
48 hours	35.869565	75%	40%	1			
	0	100%	0%	2	0.9	0.0	66.6
	0	100%	0%	3	0.0	0.0	na
	59.539474	50%	71%	4	2.0	0.1	56.0
	75	50%	81%				
	153.73665	0%	90%				

FIG. 1 - 2

Erythropoietin receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	28.716	15.032	28.716	30.854	28.716	0.517
average	178.249	40.826	178.249	51.347	178.249	0.517
stdev	1018.857	51.724	1018.857	55.625	1018.857	na
p (t-test)		0.540		0.554		na
min	0.517	0.517	0.517	0.517	0.517	0.517
max	7307.410	163.136	7307.410	190.476	7307.410	0.517
n (Samp)	51	21	51	23	51	1
n (Pat)	39	21	39	23	39	1

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	20.270	23.597	20.270	38.766	20.270	57.010
average	116.048	54.648	116.048	70.648	116.048	57.010
stdev	759.083	68.689	759.083	72.286	759.083	51.958
p (t-test)		0.844		0.875		0.913
min	0.517	0.517	0.517	0.517	0.517	20.270
max	7307.410	150.424	7307.410	190.476	7307.410	93.750
n (Samp)	92	6	92	7	92	2
n (Pat)	72	6	72	7	72	2

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	42.187	17.651	42.187	30.854	42.187	49.738
average	220.621	41.168	220.621	58.131	220.621	62.604
stdev	1120.988	49.387	1120.988	60.332	1120.988	74.707
p (t-test)		0.527		0.511		0.782
min	0.517	0.517	0.517	0.517	0.517	0.517
max	7307.410	163.136	7307.410	190.476	7307.410	150.424
n (Samp)	42	16	42	21	42	4
n (Pat)	32	16	32	21	32	4

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.47	0.075	51	21	0.698
24 hours	0.54	0.073	51	23	0.550
48 hours	0.16	0.142	51	1	0.016

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.51	0.123	92	6	0.906
24 hours	0.63	0.117	92	7	0.276
48 hours	0.69	0.211	92	2	0.360

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.42	0.082	42	16	0.319
24 hours	0.50	0.078	42	21	0.988
48 hours	0.50	0.153	42	4	0.984

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0	100%	0%	1			
	0	100%	0%	2	0.2	0.0	0.9
	0	100%	0%	3	0.3	0.1	1.1
	54.588608	33%	71%	4	1.6	0.6	3.8
	78.125	14%	80%				
	88.541667	14%	90%				
24 hours	0	100%	0%	1			

FIG. 1 - 3

	0	100%	0%	2	0.4	0.1	1.2
	0	100%	0%	3	0.6	0.2	1.6
	54.588608	39%	71%	4	0.9	0.4	2.3
	78.125	26%	80%				
	88.541667	22%	90%				
48 hours	0	100%	0%	1			
	0	100%	0%	2	na	na	na
	0	100%	0%	3	na	na	na
	54.588608	0%	71%	4	na	na	na
	78.125	0%	80%				
	88.541667	0%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0	100%	0%	1			
	0	100%	0%	2	0.5	0.0	10.3
	0	100%	0%	3	0.5	0.0	10.8
	62.5	33%	72%	4	1.0	0.1	8.1
	78.125	33%	82%				
	94.758065	33%	90%				
24 hours	28.716216	71%	55%	1			
	0	100%	0%	2	0.0	0.0	na
	0	100%	0%	3	1.0	0.1	8.1
	62.5	43%	72%	4	1.5	0.2	9.2
	78.125	43%	82%				
	94.758065	43%	90%				
48 hours	15.031646	100%	48%	1			
	15.031646	100%	48%	2	na	na	na
	15.031646	100%	48%	3	na	na	na
	62.5	50%	72%	4	na	na	na
	78.125	50%	82%				
	94.758065	0%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0	100%	0%	1			
	0	100%	0%	2	0.8	0.2	3.4
	0	100%	0%	3	0.7	0.2	3.0
	66.532258	38%	71%	4	2.1	0.6	7.1
	88.541667	13%	86%				
	109.375	13%	90%				
24 hours	7.1202532	76%	24%	1			
	0	100%	0%	2	1.2	0.4	3.6
	0	100%	0%	3	0.7	0.2	2.3
	66.532258	38%	71%	4	1.2	0.4	3.6
	88.541667	24%	86%				
	109.375	19%	90%				
48 hours	0	100%	0%	1			
	0	100%	0%	2	0.0	0.0	na
	0	100%	0%	3	0.0	0.0	na
	66.532258	50%	71%	4	0.9	0.1	9.7
	88.541667	50%	86%				
	109.375	25%	90%				

FIG. 1 - 4

Intercellular adhesion molecule 1

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	4822.109	4749.879	4822.109	4967.611	4822.109	5732.760
average	5958.736	6285.863	5958.736	7704.852	5958.736	7129.626
stdev	4520.021	4663.788	4520.021	13491.187	4520.021	5612.053
p (t-test)		0.669		0.207		0.255
min	143.975	484.285	143.975	17.651	143.975	972.754
max	20734.291	19407.277	20734.291	101592.853	20734.291	19763.346
n (Samp)	118	51	118	56	118	26
n (Pat)	99	51	99	56	99	26

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	4929.400	2340.611	4929.400	2958.798	4929.400	3794.253
average	6580.251	3663.674	6580.251	4770.984	6580.251	6101.965
stdev	7582.775	3829.021	7582.775	4498.755	7582.775	4881.287
p (t-test)		0.117		0.261		0.816
min	49.188	319.458	49.188	17.651	49.188	1667.339
max	101592.853	13756.150	101592.853	14369.565	101592.853	16638.114
n (Samp)	256	17	256	23	256	14
n (Pat)	160	17	160	23	160	14

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	4667.045	6019.775	4667.045	5663.788	4667.045	5345.772
average	5915.725	6699.792	5915.725	8485.414	5915.725	6591.910
stdev	4761.338	4578.388	4761.338	14515.055	4761.338	5384.027
p (t-test)		0.351		0.103		0.548
min	143.975	484.285	143.975	255.128	143.975	972.754
max	20734.291	19407.277	20734.291	101592.853	20734.291	19763.346
n (Samp)	106	45	106	47	106	23
n (Pat)	84	45	84	47	84	23

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.51	0.049	118	51	0.759
24 hours	0.52	0.047	118	56	0.722
48 hours	0.55	0.064	118	26	0.467

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.30	0.056	256	17	0.000
24 hours	0.38	0.057	256	23	0.035
48 hours	0.48	0.079	256	14	0.831

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.56	0.052	106	45	0.216
24 hours	0.57	0.051	106	47	0.170
48 hours	0.54	0.067	106	23	0.593

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	3117.4003	71%	34%	1			
	2243.5899	80%	19%	2	1.3	0.8	1.9
	1768.7072	90%	13%	3	0.8	0.5	1.3
	6867.8374	35%	70%	4	1.3	0.9	2.1
	9273.1411	27%	81%				
	12344.643	16%	91%				

FIG. 1 - 5

24 hours	3006.2743	71%	32%	1			
	2557.6547	80%	25%	2	1.1	0.7	1.6
	878.55325	91%	4%	3	1.0	0.6	1.5
	6867.8374	30%	70%	4	1.3	0.9	2.0
	9273.1411	25%	81%				
	12344.643	18%	91%				
48 hours	2740.7946	73%	30%	1			
	2003.1475	81%	14%	2	0.4	0.1	1.1
	1210.828	92%	9%	3	1.4	0.7	2.6
	6867.8374	35%	70%	4	1.0	0.5	2.0
	9273.1411	27%	81%				
	12344.643	19%	91%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	1815.9215	71%	15%	1			
	1747.3469	82%	14%	2	0.5	0.0	10.0
	484.28516	94%	1%	3	2.7	0.6	11.1
	7429.533	12%	70%	4	5.1	1.4	18.0
	10048.887	12%	80%				
	13216.773	6%	90%				
24 hours	1644.3701	74%	14%	1			
	1017.2784	83%	6%	2	0.6	0.2	1.8
	795.00903	91%	4%	3	1.2	0.6	2.7
	7429.533	22%	70%	4	2.0	1.0	3.8
	10048.887	17%	80%				
	13216.773	13%	90%				
48 hours	3348.3318	71%	33%	1			
	2133.882	86%	20%	2	1.0	0.3	4.0
	1774.5861	93%	14%	3	1.7	0.6	5.2
	7429.533	29%	70%	4	1.0	0.3	4.0
	10048.887	21%	80%				
	13216.773	14%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	3329.4421	71%	39%	1			
	2722.1633	80%	34%	2	1.7	1.0	2.9
	1296.436	91%	12%	3	1.3	0.7	2.3
	6539.8171	44%	71%	4	2.4	1.4	4.0
	8936.5808	33%	80%				
	13284.487	11%	91%				
24 hours	3702.7733	70%	42%	1			
	2618.5406	81%	31%	2	1.7	1.0	3.0
	878.55325	91%	7%	3	1.7	1.0	3.0
	6539.8171	43%	71%	4	2.3	1.4	4.0
	8936.5808	28%	80%				
	13284.487	11%	91%				
48 hours	3282.8748	74%	39%	1			
	2003.1475	83%	17%	2	1.0	0.4	2.5
	1210.828	91%	10%	3	1.8	0.8	4.0
	6539.8171	30%	71%	4	1.0	0.4	2.4
	8936.5808	22%	80%				
	13284.487	13%	91%				

FIG. 1 - 6

Lactotransferrin

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	39.773	50.021	39.773	39.223	39.773	37.343
average	120.491	83.370	120.491	156.989	120.491	162.414
stdev	738.191	121.800	738.191	331.383	738.191	546.410
p (t-test)		0.722		0.725		0.785
min	0.034	0.264	0.034	0.596	0.034	3.410
max	7981.395	752.000	7981.395	2143.046	7981.395	2826.490
n (Samp)	116	51	116	56	116	26
n (Pat)	98	51	98	56	98	26

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	39.773	50.517	39.773	39.968	39.773	77.168
average	129.351	53.641	129.351	165.909	129.351	96.364
stdev	561.449	35.895	561.449	439.777	561.449	80.849
p (t-test)		0.579		0.761		0.827
min	0.034	1.988	0.034	1.565	0.034	3.410
max	7981.395	104.402	7981.395	2143.046	7981.395	266.230
n (Samp)	256	17	256	23	256	14
n (Pat)	158	17	158	23	158	14

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	40.304	53.534	40.304	53.363	40.304	34.168
average	144.317	97.892	144.317	133.790	144.317	175.412
stdev	800.158	136.062	800.158	206.064	800.158	580.450
p (t-test)		0.700		0.931		0.860
min	0.034	0.264	0.034	0.596	0.034	4.872
max	7981.395	752.000	7981.395	1014.570	7981.395	2826.490
n (Samp)	105	45	105	45	105	23
n (Pat)	84	45	84	45	84	23

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.58	0.049	116	51	0.119
24 hours	0.59	0.047	116	56	0.070
48 hours	0.54	0.064	116	26	0.512

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.51	0.073	256	17	0.865
24 hours	0.54	0.064	256	23	0.577
48 hours	0.65	0.082	256	14	0.072

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.61	0.052	105	45	0.037
24 hours	0.62	0.051	105	45	0.023
48 hours	0.54	0.068	105	23	0.562

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	17.851931	71%	35%	1			
	13.620825	80%	32%	2	2.3	1.4	3.8
	9.6548571	90%	24%	3	1.5	0.8	2.5
	67.675531	43%	71%	4	2.8	1.7	4.6
	94.231339	25%	80%				
	112.67707	20%	91%				

FIG. 1 - 7

24 hours	20.639446	71%	41%	1			
	11.81696	80%	30%	2	1.9	1.2	2.9
	4.9357657	91%	10%	3	0.6	0.3	1.0
	67.675531	41%	71%	4	2.8	1.8	4.2
	94.231339	38%	80%				
	112.67707	30%	91%				
48 hours	21.915017	73%	42%	1			
	7.5921674	81%	22%	2	1.2	0.6	2.4
	4.8724396	92%	10%	3	0.8	0.3	1.9
	67.675531	38%	71%	4	1.4	0.7	2.8
	94.231339	23%	80%				
	112.67707	15%	91%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	34.168163	71%	46%	1			
	12.977528	82%	27%	2	1.0	0.3	3.9
	2.7344176	94%	6%	3	3.3	1.3	8.4
	82.278359	35%	70%	4	0.6	0.1	3.5
	110.58056	0%	80%				
	177.32683	0%	90%				
24 hours	20.639446	74%	37%	1			
	8.0510017	83%	18%	2	1.2	0.6	2.6
	5.178951	91%	11%	3	1.2	0.6	2.6
	82.278359	35%	70%	4	1.2	0.6	2.6
	110.58056	22%	80%				
	177.32683	22%	90%				
48 hours	52.373934	71%	58%	1			
	32.271515	86%	46%	2	3.0	0.2	44.1
	21.915017	93%	38%	3	5.3	0.5	59.5
	82.278359	50%	70%	4	5.2	0.5	58.5
	110.58056	29%	80%				
	177.32683	14%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	19.034353	71%	35%	1			
	16.4864	80%	32%	2	2.7	1.4	5.0
	9.728	91%	21%	3	1.7	0.8	3.3
	63.154087	47%	70%	4	4.2	2.3	7.6
	84.873371	38%	80%				
	110.58056	24%	90%				
24 hours	24.180364	71%	43%	1			
	16.4864	80%	32%	2	1.7	1.0	2.9
	7.2355165	91%	17%	3	0.8	0.4	1.6
	63.154087	47%	70%	4	3.3	1.9	5.5
	84.873371	40%	80%				
	110.58056	36%	90%				
48 hours	11.81696	74%	28%	1			
	8.37632	83%	19%	2	1.5	0.7	3.4
	5.9977143	91%	14%	3	0.6	0.2	1.8
	63.154087	39%	70%	4	1.8	0.8	4.0
	84.873371	30%	80%				
	110.58056	22%	90%				

FIG. 1 - 8

Prostatic Acid Phosphatase

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	4.495	9.470	4.495	6.460	4.495	8.710
average	24.231	33.377	24.231	40.086	24.231	24.383
stdev	70.981	66.711	70.981	96.501	70.981	48.277
p (t-test)		0.390		0.147		0.991
min	0.006	0.026	0.006	0.024	0.006	0.293
max	530.000	310.000	530.000	521.000	530.000	235.000
n (Samp)	248	53	248	62	248	27
n (Pat)	103	53	103	62	103	27

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	5.850	3.525	5.850	2.440	5.850	7.380
average	27.843	19.082	27.843	34.058	27.843	10.736
stdev	69.781	52.720	69.781	94.152	69.781	9.926
p (t-test)		0.580		0.666		0.360
min	0.006	0.000	0.006	0.104	0.006	0.057
max	530.000	237.000	530.000	469.000	530.000	31.100
n (Samp)	440	20	440	26	440	14
n (Pat)	169	20	169	26	169	14

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	3.760	10.500	3.760	8.355	3.760	6.380
average	16.262	34.131	16.262	44.849	16.262	24.810
stdev	53.571	64.385	53.571	104.231	53.571	50.431
p (t-test)		0.048		0.006		0.449
min	0.006	0.026	0.006	0.024	0.006	0.293
max	530.000	310.000	530.000	521.000	530.000	235.000
n (Samp)	212	47	212	52	212	25
n (Pat)	85	47	85	52	85	25

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.58	0.045	248	53	0.081
24 hours	0.53	0.041	248	62	0.454
48 hours	0.59	0.060	248	27	0.140

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.40	0.061	440	20	0.111
24 hours	0.45	0.056	440	26	0.372
48 hours	0.52	0.079	440	14	0.774

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.62	0.047	212	47	0.011
24 hours	0.56	0.045	212	52	0.208
48 hours	0.58	0.063	212	25	0.196

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	2.48	72%	37%	1			
	0.425	83%	13%	2	0.5	0.3	0.9
	0.158	91%	7%	3	1.2	0.8	1.7
	11.6	42%	71%	4	1.9	1.4	2.6
	18.7	36%	80%				
	41.8	19%	90%				

FIG. 1 - 9

24 hours	1.38	71%	25%	1			
	0.843	81%	20%	2	0.5	0.4	0.8
	0.471	90%	15%	3	0.5	0.3	0.7
	11.6	40%	71%	4	1.4	1.1	1.8
	18.7	29%	80%				
	41.8	19%	90%				
48 hours	3.72	70%	47%	1			
	1.2	81%	23%	2	0.5	0.2	1.3
	0.755	93%	19%	3	1.4	0.7	2.6
	11.6	41%	71%	4	1.8	1.0	3.2
	18.7	33%	80%				
	41.8	11%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	1.23	70%	23%	1			
	0.394	80%	12%	2	1.7	0.6	5.0
	0.307	90%	11%	3	1.3	0.4	4.4
	18.1	15%	70%	4	2.8	1.1	7.1
	29.8	15%	80%				
	55.9	5%	90%				
24 hours	1.38	73%	25%	1			
	1.05	85%	21%	2	1.0	0.4	2.3
	0.311	92%	11%	3	1.6	0.8	3.2
	18.1	23%	70%	4	1.7	0.8	3.3
	29.8	15%	80%				
	55.9	15%	90%				
48 hours	5.21	71%	48%	1			
	2.19	86%	32%	2	2.0	0.4	9.1
	1.38	93%	25%	3	3.1	0.8	11.9
	18.1	21%	70%	4	1.0	0.1	7.3
	29.8	7%	80%				
	55.9	0%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	2.74	70%	43%	1			
	0.471	81%	16%	2	0.5	0.3	0.9
	0.158	91%	9%	3	0.8	0.5	1.2
	9.25	55%	71%	4	2.3	1.6	3.3
	13.8	43%	80%				
	25.3	34%	90%				
24 hours	0.986	71%	22%	1			
	0.639	81%	17%	2	0.2	0.1	0.4
	0.311	90%	13%	3	0.3	0.2	0.5
	9.25	42%	71%	4	1.3	1.0	1.8
	13.8	42%	80%				
	25.3	25%	90%				
48 hours	1.74	72%	31%	1			
	1.2	80%	24%	2	0.8	0.4	1.8
	0.74	92%	20%	3	0.8	0.4	1.8
	9.25	44%	71%	4	1.6	0.8	2.9
	13.8	36%	80%				
	25.3	20%	90%				

FIG. 1 - 10

von Willebrand Factor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.006	0.009	0.006	0.011	0.006	0.010
average	0.028	0.017	0.028	0.226	0.028	0.017
stdev	0.154	0.025	0.154	1.585	0.154	0.016
p (t-test)		0.599		0.054		0.700
min	0.000	0.000	0.000	0.000	0.000	0.001
max	2.330	0.123	2.330	12.500	2.330	0.058
n (Samp)	248	53	248	62	248	27
n (Pat)	103	53	103	62	103	27

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.007	0.009	0.007	0.013	0.007	0.013
average	0.053	0.021	0.053	0.028	0.053	0.017
stdev	0.606	0.032	0.606	0.034	0.606	0.014
p (t-test)		0.815		0.830		0.826
min	0.000	0.000	0.000	0.001	0.000	0.001
max	12.500	0.123	12.500	0.162	12.500	0.045
n (Samp)	440	20	440	26	440	14
n (Pat)	169	20	169	26	169	14

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.007	0.009	0.007	0.012	0.007	0.010
average	0.031	0.018	0.031	0.263	0.031	0.019
stdev	0.166	0.024	0.166	1.730	0.166	0.021
p (t-test)		0.597		0.055		0.712
min	0.000	0.001	0.000	0.000	0.000	0.002
max	2.330	0.123	2.330	12.500	2.330	0.089
n (Samp)	212	47	212	52	212	25
n (Pat)	85	47	85	52	85	25

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.55	0.044	248	53	0.247
24 hours	0.61	0.042	248	62	0.009
48 hours	0.59	0.060	248	27	0.152

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.53	0.067	440	20	0.642
24 hours	0.63	0.060	440	26	0.035
48 hours	0.62	0.081	440	14	0.151

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.58	0.047	212	47	0.087
24 hours	0.62	0.045	212	52	0.006
48 hours	0.59	0.063	212	25	0.153

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.00501	72%	41%	1			
	0.00398	81%	35%	2	1.0	0.6	1.6
	0.00127	91%	11%	3	2.1	1.4	3.0
	0.0142	32%	70%	4	1.6	1.1	2.4
	0.019	19%	81%				
	0.049	11%	90%				

FIG. 1 - 11

24 hours	0.00598	71%	48%	1			
	0.00379	81%	33%	2	1.1	0.7	1.7
	0.00183	90%	18%	3	1.9	1.3	2.8
	0.0142	39%	70%	4	3.0	2.1	4.2
	0.019	37%	81%				
	0.049	18%	90%				
48 hours	0.00598	70%	48%	1			
	0.00334	81%	30%	2	0.8	0.3	2.0
	0.0017	93%	16%	3	1.9	1.0	3.7
	0.0142	41%	70%	4	1.9	1.0	3.7
	0.019	33%	81%				
	0.049	4%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.00517	70%	37%	1			
	0.00267	80%	21%	2	0.8	0.3	2.0
	0.00141	90%	11%	3	1.0	0.4	2.3
	0.0146	35%	70%	4	1.2	0.6	2.6
	0.0219	30%	80%				
	0.0491	10%	90%				
24 hours	0.00675	73%	46%	1			
	0.00442	81%	33%	2	1.0	0.4	2.7
	0.00183	92%	16%	3	1.5	0.7	3.6
	0.0146	46%	70%	4	3.2	1.6	6.4
	0.0219	46%	80%				
	0.0491	19%	90%				
48 hours	0.0104	71%	60%	1			
	0.00398	86%	30%	2	0.5	0.0	9.6
	0.0017	93%	15%	3	3.7	1.0	13.4
	0.0146	43%	70%	4	2.0	0.4	9.1
	0.0219	29%	80%				
	0.0491	0%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.00683	70%	51%	1			
	0.00485	81%	39%	2	1.8	1.0	3.2
	0.00127	91%	10%	3	3.4	2.0	5.7
	0.0144	36%	70%	4	2.7	1.5	4.5
	0.0227	19%	81%				
	0.0457	11%	90%				
24 hours	0.0071	71%	53%	1			
	0.00485	81%	39%	2	1.3	0.8	2.3
	0.00226	90%	22%	3	2.7	1.7	4.3
	0.0144	44%	70%	4	3.7	2.3	5.8
	0.0227	29%	81%				
	0.0457	15%	90%				
48 hours	0.00598	72%	47%	1			
	0.00403	80%	33%	2	1.7	0.6	5.3
	0.00208	92%	17%	3	3.4	1.3	8.6
	0.0144	40%	70%	4	2.9	1.1	7.6
	0.0227	28%	81%				
	0.0457	12%	90%				

FIG. 1 - 12

Endothelial protein C receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	50.329	0.068	50.329	60.949	50.329	0.068
average	72.893	8.232	72.893	83.497	72.893	36.786
stdev	73.245	na	73.245	62.004	73.245	na
p (t-test)		na		0.586		na
min	0.068	8.232	0.068	25.357	0.068	36.786
max	491.892	8.232	491.892	258.333	491.892	36.786
n (Samp)	95	1	95	16	95	1
n (Pat)	73	1	73	16	73	1

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	54.309	na	54.309	55.000	54.309	na
average	74.596	na	74.596	68.999	74.596	na
stdev	71.935	na	71.935	52.073	71.935	na
p (t-test)		na		0.894		na
min	0.068	na	0.068	25.357	0.068	na
max	491.892	na	491.892	126.641	491.892	na
n (Samp)	110	0	110	3	110	0
n (Pat)	86	0	86	3	86	0

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	52.771	0.068	52.771	64.803	52.771	45.893
average	74.160	8.232	74.160	151.262	74.160	45.893
stdev	77.373	na	77.373	246.285	77.373	12.879
p (t-test)		na		0.025		0.609
min	0.068	8.232	0.068	28.623	0.068	36.786
max	491.892	8.232	491.892	1013.333	491.892	55.000
n (Samp)	78	1	78	15	78	2
n (Pat)	60	1	60	15	60	2

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.02	0.025	95	1	0.000
24 hours	0.60	0.080	95	16	0.204
48 hours	0.37	0.254	95	1	0.604

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	nd	nd	110	0	nd
24 hours	0.52	0.171	110	3	0.916
48 hours	nd	nd	110	0	nd

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.03	0.031	78	1	0.000
24 hours	0.66	0.082	78	15	0.054
48 hours	0.45	0.199	78	2	0.785

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.9615385	100%	2%	1			
	0.9615385	100%	2%	2	na	na	na
	0.9615385	100%	2%	3	na	na	na
	80.384615	0%	71%	4	na	na	na
	105.01931	0%	81%				
	158.30116	0%	91%				

FIG. 2 - 1

24 hours	47.463768	75%	47%	1			
	35.869565	81%	37%	2	1.5	0.3	9.0
	28.214286	94%	26%	3	4.2	1.0	17.4
	80.384615	38%	71%	4	2.1	0.4	10.6
	105.01931	25%	81%				
	158.30116	13%	91%				
48 hours	35.869565	100%	37%	1			
	35.869565	100%	37%	2	na	na	na
	35.869565	100%	37%	3	na	na	na
	80.384615	0%	71%	4	na	na	na
	105.01931	0%	81%				
	158.30116	0%	91%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	na	na	na	1			
	na	na	na	2	na	na	na
	na	na	na	3	na	na	na
	na	na	na	4	na	na	na
	na	na	na				
	na	na	na				
24 hours	24.038462	100%	20%	1			
	24.038462	100%	20%	2	0.0	0.0	na
	24.038462	100%	20%	3	1.0	0.0	58.3
	81.153846	33%	70%	4	1.0	0.0	56.0
	105.01931	33%	80%				
	158.30116	0%	90%				
48 hours	na	na	na	1			
	na	na	na	2	na	na	na
	na	na	na	3	na	na	na
	na	na	na	4	na	na	na
	na	na	na				
	na	na	na				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	2.8846154	100%	3%	1			
	2.8846154	100%	3%	2	na	na	na
	2.8846154	100%	3%	3	na	na	na
	80.384615	0%	71%	4	na	na	na
	105.01931	0%	81%				
	158.30116	0%	91%				
24 hours	56.25	73%	55%	1			
	47.463768	80%	46%	2	3.3	0.2	54.3
	28.623188	93%	28%	3	7.8	0.6	93.8
	80.384615	47%	71%	4	5.8	0.5	73.7
	105.01931	33%	81%				
	158.30116	20%	91%				
48 hours	35.869565	100%	36%	1			
	35.869565	100%	36%	2	na	na	na
	35.869565	100%	36%	3	na	na	na
	80.384615	0%	71%	4	na	na	na
	105.01931	0%	81%				
	158.30116	0%	91%				

FIG. 2 - 2

Erythropoietin receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	20.270	0.517	20.270	91.146	20.270	0.517
average	112.572	94.758	112.572	86.707	112.572	98.958
stdev	739.437	na	739.437	60.643	739.437	na
p (t-test)		na		0.889		na
min	0.517	94.758	0.517	0.517	0.517	98.958
max	7307.410	94.758	7307.410	180.085	7307.410	98.958
n (Samp)	97	1	97	16	97	1
n (Pat)	73	1	73	16	73	1

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	28.716	na	28.716	104.167	28.716	na
average	108.007	na	108.007	88.086	108.007	na
stdev	688.107	na	688.107	51.125	688.107	na
p (t-test)		na		0.960		na
min	0.517	na	0.517	30.854	0.517	na
max	7307.410	na	7307.410	129.237	7307.410	na
n (Samp)	112	0	112	3	112	0
n (Pat)	86	0	86	3	86	0

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	28.716	0.517	28.716	88.542	28.716	64.906
average	132.319	94.758	132.319	83.871	132.319	64.906
stdev	813.620	na	813.620	61.664	813.620	48.157
p (t-test)		na		0.819		0.908
min	0.517	94.758	0.517	0.517	0.517	30.854
max	7307.410	94.758	7307.410	180.085	7307.410	98.958
n (Samp)	80	1	80	15	80	2
n (Pat)	60	1	60	15	60	2

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.90	0.210	97	1	0.059
24 hours	0.74	0.075	97	16	0.002
48 hours	0.90	0.206	97	1	0.051

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	nd	nd	112	0	nd
24 hours	0.78	0.160	112	3	0.080
48 hours	nd	nd	112	0	nd

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.88	0.228	80	1	0.099
24 hours	0.70	0.080	80	15	0.013
48 hours	0.70	0.210	80	2	0.334

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	90.725806	100%	90%	1			
	90.725806	100%	90%	2	na	na	na
	90.725806	100%	90%	3	na	na	na
	54.054054	100%	70%	4	na	na	na
	74.596774	100%	80%				
	98.958333	0%	91%				
24 hours	28.716216	75%	56%	1			

FIG. 2 - 3

	22.943038	81%	53%	2	1.0	0.1	8.3
	0	100%	0%	3	1.6	0.3	9.3
	54.054054	69%	70%	4	5.9	1.5	23.0
	74.596774	56%	80%				
	98.958333	44%	91%				
48 hours	90.725806	100%	90%	1			
	90.725806	100%	90%	2	na	na	na
	90.725806	100%	90%	3	na	na	na
	54.054054	100%	70%	4	na	na	na
	74.596774	100%	80%				
	98.958333	0%	91%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	88.541667	100%	88%	1			
	88.541667	100%	88%	2	na	na	na
	88.541667	100%	88%	3	na	na	na
	62.5	100%	73%	4	na	na	na
	78.125	100%	81%				
	109.375	0%	90%				
24 hours	28.716216	73%	51%	1			
	22.943038	80%	49%	2	1.5	0.2	9.3
	0	100%	0%	3	1.0	0.1	8.1
	62.5	67%	73%	4	5.3	1.2	22.2
	78.125	53%	81%				
	109.375	33%	90%				
48 hours	28.716216	100%	51%	1			
	28.716216	100%	51%	2	na	na	na
	28.716216	100%	51%	3	na	na	na
	62.5	50%	73%	4	na	na	na
	78.125	50%	81%				
	109.375	0%	90%				

FIG. 2 - 4

Intercellular adhesion molecule 1

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	4749.879	5068.987	4749.879	3830.843	4749.879	4278.585
average	6133.036	5108.270	6133.036	7776.837	6133.036	4365.820
stdev	4859.623	2684.272	4859.623	16847.250	4859.623	3439.120
p (t-test)		0.320		0.222		0.154
min	143.975	49.188	143.975	17.651	143.975	884.006
max	23945.523	9162.750	23945.523	101592.853	23945.523	12963.420
n (Samp)	247	23	247	35	247	16
n (Pat)	161	23	161	35	161	16

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	4756.924	3271.166	4756.924	6266.884	4756.924	1770.488
average	6280.964	3271.166	6280.964	7081.972	6280.964	2457.922
stdev	7095.695	2542.503	7095.695	5657.135	7095.695	1491.164
p (t-test)		0.550		0.752		0.156
min	49.188	1473.344	49.188	17.651	49.188	932.744
max	101592.853	5068.987	101592.853	14369.565	101592.853	4811.596
n (Samp)	316	2	316	8	316	7
n (Pat)	190	2	190	8	190	7

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	4891.600	5046.487	4891.600	3741.190	4891.600	5207.380
average	6284.356	5134.771	6284.356	7825.788	6284.356	5386.829
stdev	4926.338	2639.694	4926.338	18122.796	4926.338	3921.802
p (t-test)		0.272		0.313		0.505
min	143.975	49.188	143.975	255.128	143.975	884.006
max	23945.523	9162.750	23945.523	101592.853	23945.523	12963.420
n (Samp)	212	23	212	30	212	14
n (Pat)	133	23	133	30	133	14

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.49	0.063	247	23	0.885
24 hours	0.45	0.051	247	35	0.300
48 hours	0.40	0.068	247	16	0.136

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.33	0.168	316	2	0.317
24 hours	0.55	0.106	316	8	0.625
48 hours	0.24	0.073	316	7	0.000

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.48	0.063	212	23	0.802
24 hours	0.41	0.053	212	30	0.106
48 hours	0.46	0.078	212	14	0.640

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	3708.0684	74%	41%	1			
	1837.2172	83%	16%	2	3.8	1.5	9.5
	1404.7125	91%	13%	3	1.7	0.6	5.2
	7384.4411	22%	70%	4	1.7	0.6	5.3
	10095.697	0%	80%				
	13351.36	0%	90%				

FIG. 2 - 5

24 hours	2425.248	71%	23%	1			
	1193.0554	80%	11%	2	1.0	0.6	1.8
	808.35928	91%	6%	3	1.0	0.6	1.7
	7384.4411	26%	70%	4	1.5	0.9	2.4
	10095.697	20%	80%				
	13351.36	9%	90%				
48 hours	1648.5508	75%	14%	1			
	1106.0835	81%	10%	2	3.2	0.8	12.6
	884.00556	94%	6%	3	1.0	0.1	7.5
	7384.4411	13%	70%	4	3.3	0.8	12.8
	10095.697	13%	80%				
	13351.36	0%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	1404.7125	100%	13%	1			
	1404.7125	100%	13%	2	na	na	na
	1404.7125	100%	13%	3	na	na	na
	7088.3129	0%	70%	4	na	na	na
	9642.0131	0%	80%				
	13216.773	0%	90%				
24 hours	3348.3318	75%	37%	1			
	884.00556	88%	6%	2	0.5	0.0	9.8
	0	100%	0%	3	1.0	0.1	7.5
	7088.3129	50%	70%	4	1.5	0.3	8.2
	9642.0131	38%	80%				
	13216.773	25%	90%				
48 hours	1648.5508	71%	15%	1			
	1017.2784	86%	8%	2	na	na	na
	884.00556	100%	6%	3	na	na	na
	7088.3129	0%	70%	4	na	na	na
	9642.0131	0%	80%				
	13216.773	0%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	3708.0684	74%	39%	1			
	2243.5899	83%	21%	2	3.4	1.3	8.6
	1747.3469	91%	14%	3	2.1	0.7	6.1
	7577.8005	22%	70%	4	1.8	0.6	5.4
	10218.757	0%	80%				
	13463.237	0%	90%				
24 hours	2425.248	70%	22%	1			
	1404.7125	80%	12%	2	1.0	0.5	2.1
	878.55325	90%	7%	3	1.0	0.5	2.1
	7577.8005	20%	70%	4	2.3	1.3	4.0
	10218.757	10%	80%				
	13463.237	7%	90%				
48 hours	2797.6993	71%	29%	1			
	1106.0835	86%	9%	2	1.8	0.6	5.4
	884.00556	93%	7%	3	0.7	0.1	3.6
	7577.8005	21%	70%	4	1.4	0.4	4.7
	10218.757	14%	80%				
	13463.237	0%	90%				

FIG. 2 - 6

Lactotransferrin

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	36.887	78.341	36.887	82.075	36.887	88.387
average	119.269	83.910	119.269	232.803	119.269	91.862
stdev	565.405	69.613	565.405	475.549	565.405	71.532
p (t-test)		0.765		0.259		0.838
min	0.034	0.264	0.034	0.596	0.034	1.598
max	7981.395	287.712	7981.395	2508.696	7981.395	252.566
n (Samp)	241	23	241	35	241	18
n (Pat)	158	23	158	35	158	18

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	43.590	88.709	43.590	45.749	43.590	88.688
average	126.727	88.709	126.727	40.853	126.727	120.099
stdev	522.076	0.654	522.076	29.906	522.076	90.032
p (t-test)		0.918		0.643		0.973
min	0.034	88.246	0.034	1.565	0.034	3.410
max	7981.395	89.171	7981.395	82.075	7981.395	252.566
n (Samp)	313	2	313	8	313	7
n (Pat)	187	2	187	8	187	7

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	38.710	74.540	38.710	97.471	38.710	88.629
average	128.634	81.854	128.634	266.228	128.634	87.749
stdev	608.641	69.977	608.641	506.904	608.641	59.278
p (t-test)		0.713		0.239		0.789
min	0.034	0.264	0.034	0.596	0.034	1.598
max	7981.395	287.712	7981.395	2508.696	7981.395	223.790
n (Samp)	207	23	207	30	207	16
n (Pat)	131	23	131	30	131	16

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.63	0.065	241	23	0.047
24 hours	0.66	0.053	241	35	0.002
48 hours	0.66	0.072	241	18	0.027

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.73	0.205	313	2	0.271
24 hours	0.43	0.098	313	8	0.489
48 hours	0.69	0.113	313	7	0.098

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.61	0.065	207	23	0.079
24 hours	0.70	0.056	207	30	0.000
48 hours	0.68	0.076	207	16	0.021

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	41.916484	74%	54%	1			
	15.01184	83%	32%	2	0.5	0.1	2.2
	3.4238654	91%	7%	3	1.6	0.6	3.7
	69.14188	65%	70%	4	3.1	1.5	6.5
	94.924245	30%	80%				
	156.83453	13%	90%				

FIG. 2 - 7

24 hours	52.12679	71%	62%	1			
	24.630132	80%	42%	2	0.6	0.3	1.6
	7.4496546	91%	17%	3	1.8	1.0	3.2
	69.14188	51%	70%	4	2.9	1.7	4.9
	94.924245	43%	80%				
	156.83453	34%	90%				
48 hours	33.016242	72%	48%	1			
	22.047347	83%	40%	2	2.0	0.4	9.4
	2.9045645	94%	6%	3	1.0	0.1	7.4
	69.14188	56%	70%	4	5.6	1.6	19.5
	94.924245	44%	80%				
	156.83453	17%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	88.086243	100%	72%	1			
	88.086243	100%	72%	2	na	na	na
	88.086243	100%	72%	3	na	na	na
	84.665922	100%	70%	4	na	na	na
	110.58056	0%	80%				
	184.36697	0%	90%				
24 hours	17.59232	75%	31%	1			
	8.0084875	88%	17%	2	na	na	na
	1.4945818	100%	3%	3	na	na	na
	84.665922	0%	70%	4	na	na	na
	110.58056	0%	80%				
	184.36697	0%	90%				
48 hours	83.266935	71%	70%	1			
	58.662081	86%	60%	2	0.0	0.0	na
	2.9045645	100%	6%	3	3.1	0.2	44.2
	84.665922	57%	70%	4	3.1	0.2	44.2
	110.58056	43%	80%				
	184.36697	29%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	41.916484	74%	54%	1			
	15.01184	83%	30%	2	0.5	0.1	2.2
	3.4238654	91%	6%	3	2.2	1.0	4.9
	69.14188	61%	70%	4	2.4	1.1	5.3
	95.209739	30%	80%				
	156.83453	13%	90%				
24 hours	53.431061	70%	62%	1			
	28.599824	80%	44%	2	0.7	0.2	2.5
	10.71104	90%	21%	3	2.2	1.0	4.8
	69.14188	60%	70%	4	4.6	2.3	9.2
	95.209739	50%	80%				
	156.83453	40%	90%				
48 hours	33.016242	75%	47%	1			
	31.526788	81%	46%	2	4.2	0.3	51.8
	18.226171	94%	34%	3	4.2	0.3	51.8
	69.14188	56%	70%	4	7.7	0.8	78.2
	95.209739	44%	80%				
	156.83453	13%	90%				

FIG. 2 - 8

Prostatic Acid Phosphatase

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	4.770	9.470	4.770	7.160	4.770	8.725
average	22.695	31.702	22.695	54.991	22.695	30.405
stdev	60.788	88.857	60.788	126.579	60.788	49.347
p (t-test)		0.470		0.007		0.596
min	0.000	0.018	0.000	0.000	0.000	0.024
max	530.000	469.000	530.000	521.000	530.000	165.000
n (Samp)	419	27	419	36	419	18
n (Pat)	164	27	164	36	164	18

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	5.660	0.728	5.660	0.377	5.660	6.520
average	26.063	2.601	26.063	15.381	26.063	71.118
stdev	65.744	3.002	65.744	29.041	65.744	175.497
p (t-test)		0.426		0.627		0.082
min	0.000	0.311	0.000	0.000	0.000	0.057
max	530.000	6.970	530.000	89.100	530.000	469.000
n (Samp)	518	5	518	9	518	7
n (Pat)	199	5	199	9	199	7

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	4.345	12.150	4.345	6.375	4.345	8.725
average	18.404	37.135	18.404	61.630	18.404	33.471
stdev	49.284	91.191	49.284	137.322	49.284	51.687
p (t-test)		0.083		0.000		0.233
min	0.000	0.018	0.000	0.051	0.000	0.024
max	530.000	469.000	530.000	521.000	530.000	165.000
n (Samp)	352	26	352	30	352	16
n (Pat)	133	26	133	30	133	16

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.56	0.059	419	27	0.325
24 hours	0.50	0.050	419	36	0.927
48 hours	0.59	0.072	419	18	0.192

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.28	0.095	518	5	0.021
24 hours	0.37	0.085	518	9	0.122
48 hours	0.47	0.107	518	7	0.755

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.62	0.061	352	26	0.045
24 hours	0.53	0.056	352	30	0.591
48 hours	0.62	0.076	352	16	0.128

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	2.29	70%	35%	1			
	0.803	81%	19%	2	0.6	0.2	1.2
	0.471	93%	14%	3	0.8	0.4	1.6
	12.3	44%	70%	4	1.5	0.9	2.4
	21.6	37%	80%				
	45.4	7%	90%				

FIG. 2 - 9

24 hours	0.669	72%	16%	1			
	0.307	81%	10%	2	0.3	0.1	0.6
	0.102	92%	5%	3	0.5	0.3	0.8
	12.3	42%	70%	4	0.9	0.6	1.3
	21.6	28%	80%				
	45.4	19%	90%				
48 hours	6.36	72%	57%	1			
	2.29	83%	35%	2	0.3	0.0	4.6
	0.0539	94%	4%	3	3.2	1.3	7.9
	12.3	33%	70%	4	1.7	0.6	5.0
	21.6	28%	80%				
	45.4	17%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.471	80%	14%	1			
	0.471	80%	14%	2	na	na	na
	0.307	100%	10%	3	na	na	na
	15.7	0%	70%	4	na	na	na
	27.9	0%	80%				
	55.9	0%	90%				
24 hours	0.158	78%	7%	1			
	0.102	89%	5%	2	1.0	0.1	7.3
	0	100%	0%	3	0.0	0.0	na
	15.7	22%	70%	4	2.6	0.6	10.5
	27.9	11%	80%				
	55.9	11%	90%				
48 hours	1.4	71%	25%	1			
	1.23	86%	23%	2	3.1	0.2	43.2
	0.0539	100%	4%	3	1.0	0.0	52.3
	15.7	14%	70%	4	2.0	0.1	39.6
	27.9	14%	80%				
	55.9	14%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	2.32	73%	37%	1			
	1.81	81%	32%	2	0.8	0.3	2.0
	0.795	92%	20%	3	1.2	0.6	2.6
	11.7	54%	70%	4	2.3	1.3	4.3
	20.3	42%	80%				
	40.9	15%	90%				
24 hours	0.843	70%	20%	1			
	0.322	80%	11%	2	0.4	0.2	0.8
	0.186	90%	9%	3	0.5	0.3	0.9
	11.7	40%	70%	4	1.1	0.7	1.7
	20.3	33%	80%				
	40.9	20%	90%				
48 hours	5.07	75%	54%	1			
	2.29	81%	37%	2	0.3	0.0	4.6
	0.471	94%	15%	3	2.4	0.9	6.5
	11.7	44%	70%	4	1.7	0.6	5.1
	20.3	31%	80%				
	40.9	25%	90%				

FIG. 2 - 10

von Willebrand Factor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.007	0.010	0.007	0.010	0.007	0.013
average	0.023	0.016	0.023	0.387	0.023	0.034
stdev	0.119	0.019	0.119	2.078	0.119	0.058
p (t-test)		0.765		0.000		0.697
min	0.000	0.000	0.000	0.000	0.000	0.001
max	2.330	0.090	2.330	12.500	2.330	0.253
n (Samp)	419	27	419	36	419	18
n (Pat)	164	27	164	36	164	18

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.008	0.013	0.008	0.009	0.008	0.043
average	0.048	0.015	0.048	0.032	0.048	0.062
stdev	0.559	0.011	0.559	0.051	0.559	0.088
p (t-test)		0.894		0.934		0.947
min	0.000	0.000	0.000	0.002	0.000	0.002
max	12.500	0.031	12.500	0.162	12.500	0.253
n (Samp)	518	5	518	9	518	7
n (Pat)	199	5	199	9	199	7

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.007	0.010	0.007	0.013	0.007	0.013
average	0.025	0.018	0.025	0.456	0.025	0.021
stdev	0.130	0.019	0.130	2.277	0.130	0.018
p (t-test)		0.760		0.000		0.888
min	0.000	0.000	0.000	0.000	0.000	0.001
max	2.330	0.090	2.330	12.500	2.330	0.058
n (Samp)	352	26	352	30	352	16
n (Pat)	133	26	133	30	133	16

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.59	0.059	419	27	0.139
24 hours	0.63	0.052	419	36	0.013
48 hours	0.66	0.071	419	18	0.027

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.57	0.134	518	5	0.612
24 hours	0.60	0.101	518	9	0.319
48 hours	0.72	0.110	518	7	0.045

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.61	0.061	352	26	0.079
24 hours	0.63	0.056	352	30	0.022
48 hours	0.65	0.076	352	16	0.050

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.00675	70%	49%	1			
	0.00648	81%	48%	2	2.4	0.9	6.3
	0.00117	93%	10%	3	3.2	1.3	7.9
	0.014	33%	70%	4	2.8	1.1	7.1
	0.0202	19%	80%				
	0.0436	7%	90%				

FIG. 2 - 11

24 hours	0.0068	72%	49%	1			
	0.00513	81%	39%	2	1.0	0.5	2.0
	0.00183	92%	17%	3	1.5	0.9	2.7
	0.014	47%	70%	4	2.7	1.6	4.4
	0.0202	42%	80%				
	0.0436	28%	90%				
48 hours	0.0072	72%	51%	1			
	0.006	83%	46%	2	0.7	0.1	3.5
	0.0017	94%	16%	3	1.7	0.6	5.0
	0.014	44%	70%	4	2.8	1.1	7.1
	0.0202	44%	80%				
	0.0436	22%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.00945	80%	56%	1			
	0.00945	80%	56%	2	0.0	0.0	na
	0	100%	0%	3	2.0	0.1	39.0
	0.0153	40%	70%	4	2.0	0.1	39.0
	0.0232	20%	80%				
	0.049	0%	90%				
24 hours	0.00688	78%	46%	1			
	0.00317	89%	22%	2	0.5	0.0	9.6
	0.00183	100%	15%	3	1.0	0.1	7.3
	0.0153	44%	70%	4	2.0	0.4	9.0
	0.0232	33%	80%				
	0.049	22%	90%				
48 hours	0.0121	71%	64%	1			
	0.00969	86%	57%	2	0.0	0.0	na
	0.0017	100%	14%	3	2.0	0.1	39.3
	0.0153	57%	70%	4	4.1	0.3	48.5
	0.0232	57%	80%				
	0.049	29%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.00675	73%	47%	1			
	0.00665	81%	47%	2	3.7	1.0	13.5
	0.0049	92%	37%	3	4.3	1.2	15.2
	0.0143	35%	70%	4	4.8	1.4	16.7
	0.0214	23%	80%				
	0.0436	8%	90%				
24 hours	0.00745	70%	52%	1			
	0.00513	83%	38%	2	1.3	0.5	3.2
	0.00269	90%	22%	3	2.1	1.0	4.6
	0.0143	50%	70%	4	3.6	1.8	7.1
	0.0214	40%	80%				
	0.0436	27%	90%				
48 hours	0.0072	75%	50%	1			
	0.00695	81%	49%	2	1.5	0.3	8.1
	0.0023	94%	21%	3	2.0	0.5	9.3
	0.0143	44%	70%	4	3.7	1.0	13.7
	0.0214	44%	80%				
	0.0436	19%	90%				

FIG. 2 - 12

Endothelial protein C receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	65.789	55.769	65.789	55.769	65.789	55.769
average	79.393	74.076	79.393	74.076	79.393	74.076
stdev	66.381	74.076	66.381	74.076	66.381	74.076
p (t-test)		0.838		0.838		0.838
min	14.329	2.885	14.329	2.885	14.329	2.885
max	266.981	258.333	266.981	258.333	266.981	258.333
n (Samp)	24	10	24	10	24	10
n (Pat)	24	10	24	10	24	10

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	39.226	25.357	39.226	25.357	39.226	25.357
average	74.570	27.747	74.570	27.747	74.570	27.747
stdev	82.989	26.140	82.989	26.140	82.989	26.140
p (t-test)		0.376		0.376		0.376
min	14.329	2.885	14.329	2.885	14.329	2.885
max	258.333	55.000	258.333	55.000	258.333	55.000
n (Samp)	8	3	8	3	8	3
n (Pat)	8	3	8	3	8	3

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	76.597	58.462	76.597	58.462	76.597	58.462
average	89.110	64.626	89.110	64.626	89.110	64.626
stdev	70.747	40.191	70.747	40.191	70.747	40.191
p (t-test)		0.433		0.433		0.433
min	21.189	15.705	21.189	15.705	21.189	15.705
max	266.981	130.502	266.981	130.502	266.981	130.502
n (Samp)	18	6	18	6	18	6
n (Pat)	18	6	18	6	18	6

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.48	0.109	24	10	0.819
24 hours	0.48	0.109	24	10	0.819
48 hours	0.48	0.109	24	10	0.819

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.33	0.181	8	3	0.358
24 hours	0.33	0.181	8	3	0.358
48 hours	0.33	0.181	8	3	0.358

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.44	0.135	18	6	0.682
24 hours	0.44	0.135	18	6	0.682
48 hours	0.44	0.135	18	6	0.682

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	36.785714	70%	38%	1			
	33.695652	80%	38%	2	1.2	0.1	15.2
	14.329268	90%	4%	3	2.8	0.3	23.8
	81.923077	30%	71%	4	1.2	0.1	15.2
	124.55516	20%	83%				

FIG. 3 - 1

	148.26255	10%	92%				
24 hours	36.785714	70%	38%	1			
	33.695652	80%	38%	2	1.2	0.1	15.2
	14.329268	90%	4%	3	2.8	0.3	23.8
	81.923077	30%	71%	4	1.2	0.1	15.2
	124.55516	20%	83%				
	148.26255	10%	92%				
48 hours	36.785714	70%	38%	1			
	33.695652	80%	38%	2	1.2	0.1	15.2
	14.329268	90%	4%	3	2.8	0.3	23.8
	81.923077	30%	71%	4	1.2	0.1	15.2
	124.55516	20%	83%				
	148.26255	10%	92%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	33.695652	83%	33%	1			
	33.695652	83%	33%	2	1.0	0.0	110.4
	0	100%	0%	3	5.0	0.1	194.0
	105.01931	17%	72%	4	1.0	0.0	110.4
	129.53737	17%	83%				
	238.67925	0%	94%				
24 hours	33.695652	83%	33%	1			
	33.695652	83%	33%	2	1.0	0.0	110.4
	0	100%	0%	3	5.0	0.1	194.0
	105.01931	17%	72%	4	1.0	0.0	110.4
	129.53737	17%	83%				
	238.67925	0%	94%				
48 hours	33.695652	83%	33%	1			
	33.695652	83%	33%	2	1.0	0.0	110.4
	0	100%	0%	3	5.0	0.1	194.0
	105.01931	17%	72%	4	1.0	0.0	110.4
	129.53737	17%	83%				
	238.67925	0%	94%				

FIG. 3 - 2

Erythropoietin receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	20.270	88.542	20.270	88.542	20.270	88.542
average	41.677	82.893	41.677	82.893	41.677	82.893
stdev	52.703	70.492	52.703	70.492	52.703	70.492
p (t-test)		0.067		0.067		0.067
min	0.517	0.517	0.517	0.517	0.517	0.517
max	190.476	180.085	190.476	180.085	190.476	180.085
n (Samp)	25	10	25	10	25	10
n (Pat)	25	10	25	10	25	10

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	98.958	30.854	98.958	30.854	98.958	30.854
average	96.567	53.536	96.567	53.536	96.567	53.536
stdev	72.469	67.291	72.469	67.291	72.469	67.291
p (t-test)		0.388		0.388		0.388
min	0.517	0.517	0.517	0.517	0.517	0.517
max	190.476	129.237	190.476	129.237	190.476	129.237
n (Samp)	9	3	9	3	9	3
n (Pat)	9	3	9	3	9	3

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	15.032	94.506	15.032	94.506	15.032	94.506
average	25.104	86.419	25.104	86.419	25.104	86.419
stdev	29.731	71.343	29.731	71.343	29.731	71.343
p (t-test)		0.006		0.006		0.006
min	0.517	0.517	0.517	0.517	0.517	0.517
max	78.125	163.136	78.125	163.136	78.125	163.136
n (Samp)	18	6	18	6	18	6
n (Pat)	18	6	18	6	18	6

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.69	0.105	25	10	0.078
24 hours	0.69	0.105	25	10	0.078
48 hours	0.69	0.105	25	10	0.078

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.30	0.168	9	3	0.225
24 hours	0.30	0.168	9	3	0.225
48 hours	0.30	0.168	9	3	0.225

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.77	0.124	18	6	0.030
24 hours	0.77	0.124	18	6	0.030
48 hours	0.77	0.124	18	6	0.030

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	28.716216	70%	60%	1			
	3.3783784	80%	40%	2	2.0	0.1	66.2
	0	100%	0%	3	2.0	0.1	66.2
	66.532258	60%	72%	4	8.8	0.4	198.6
	72.916667	60%	80%				
	134.92063	30%	92%				
24 hours	28.716216	70%	60%	1			

FIG. 3 - 3

	3.3783784	80%	40%	2	2.0	0.1	66.2
	0	100%	0%	3	2.0	0.1	66.2
	66.532258	60%	72%	4	8.8	0.4	198.6
	72.916667	60%	80%				
	134.92063	30%	92%				
48 hours	28.716216	70%	60%	1			
	3.3783784	80%	40%	2	2.0	0.1	66.2
	0	100%	0%	3	2.0	0.1	66.2
	66.532258	60%	72%	4	8.8	0.4	198.6
	72.916667	60%	80%				
	134.92063	30%	92%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	3.3783784	83%	44%	1			
	3.3783784	83%	44%	2	1.0	0.0	110.4
	0	100%	0%	3	0.0	0.0	na
	28.716216	67%	72%	4	10.0	0.2	457.0
	70.564516	67%	83%				
	74.596774	67%	94%				
24 hours	3.3783784	83%	44%	1			
	3.3783784	83%	44%	2	1.0	0.0	110.4
	0	100%	0%	3	0.0	0.0	na
	28.716216	67%	72%	4	10.0	0.2	457.0
	70.564516	67%	83%				
	74.596774	67%	94%				
48 hours	3.3783784	83%	44%	1			
	3.3783784	83%	44%	2	1.0	0.0	110.4
	0	100%	0%	3	0.0	0.0	na
	28.716216	67%	72%	4	10.0	0.2	457.0
	70.564516	67%	83%				
	74.596774	67%	94%				

FIG. 3 - 4

Lactotransferrin

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	31.489	85.077	31.489	85.077	31.489	85.077
average	71.516	351.569	71.516	351.569	71.516	351.569
stdev	120.120	883.335	120.120	883.335	120.120	883.335
p (t-test)		0.027		0.027		0.027
min	1.495	5.878	1.495	5.878	1.495	5.878
max	752.000	3665.116	752.000	3665.116	752.000	3665.116
n (Samp)	52	23	52	23	52	23
n (Pat)	52	23	52	23	52	23

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	47.787	73.616	47.787	73.616	47.787	73.616
average	59.591	60.577	59.591	60.577	59.591	60.577
stdev	57.139	33.877	57.139	33.877	57.139	33.877
p (t-test)		0.974		0.974		0.974
min	1.988	11.345	1.988	11.345	1.988	11.345
max	223.790	83.729	223.790	83.729	223.790	83.729
n (Samp)	19	4	19	4	19	4
n (Pat)	19	4	19	4	19	4

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	31.527	86.581	31.527	86.581	31.527	86.581
average	87.231	419.668	87.231	419.668	87.231	419.668
stdev	140.053	992.504	140.053	992.504	140.053	992.504
p (t-test)		0.034		0.034		0.034
min	1.495	5.878	1.495	5.878	1.495	5.878
max	752.000	3665.116	752.000	3665.116	752.000	3665.116
n (Samp)	43	18	43	18	43	18
n (Pat)	43	18	43	18	43	18

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.68	0.070	52	23	0.011
24 hours	0.68	0.070	52	23	0.011
48 hours	0.68	0.070	52	23	0.011

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.55	0.165	19	4	0.749
24 hours	0.55	0.165	19	4	0.749
48 hours	0.55	0.165	19	4	0.749

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.66	0.080	43	18	0.041
24 hours	0.66	0.080	43	18	0.041
48 hours	0.66	0.080	43	18	0.041

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	28.599824	74%	48%	1			
	17.732181	83%	37%	2	1.3	0.3	5.4
	10.77248	91%	19%	3	2.3	0.7	8.1
	73.751891	57%	71%	4	5.6	1.7	18.4
	87.329391	48%	81%				
	165.77561	22%	90%				

FIG. 3 - 5

24 hours	28.599824	74%	48%	1			
	17.732181	83%	37%	2	1.3	0.3	5.4
	10.77248	91%	19%	3	2.3	0.7	8.1
	73.751891	57%	71%	4	5.6	1.7	18.4
	87.329391	48%	81%				
	165.77561	22%	90%				
48 hours	28.599824	74%	48%	1			
	17.732181	83%	37%	2	1.3	0.3	5.4
	10.77248	91%	19%	3	2.3	0.7	8.1
	73.751891	57%	71%	4	5.6	1.7	18.4
	87.329391	48%	81%				
	165.77561	22%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	63.548753	75%	68%	1			
	2.9045645	100%	11%	2	0.0	0.0	na
	2.9045645	100%	11%	3	2.0	0.0	100.8
	83.266935	25%	74%	4	0.8	0.0	97.4
	101.34903	0%	84%				
	156.1488	0%	95%				
24 hours	63.548753	75%	68%	1			
	2.9045645	100%	11%	2	0.0	0.0	na
	2.9045645	100%	11%	3	2.0	0.0	100.8
	83.266935	25%	74%	4	0.8	0.0	97.4
	101.34903	0%	84%				
	156.1488	0%	95%				
48 hours	63.548753	75%	68%	1			
	2.9045645	100%	11%	2	0.0	0.0	na
	2.9045645	100%	11%	3	2.0	0.0	100.8
	83.266935	25%	74%	4	0.8	0.0	97.4
	101.34903	0%	84%				
	156.1488	0%	95%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	50.765576	72%	63%	1			
	19.556624	83%	40%	2	1.6	0.2	11.4
	10.28096	94%	19%	3	5.7	1.1	29.8
	76.363749	61%	72%	4	3.9	0.7	20.4
	114.28351	33%	81%				
	190.67626	22%	91%				
24 hours	50.765576	72%	63%	1			
	19.556624	83%	40%	2	1.6	0.2	11.4
	10.28096	94%	19%	3	5.7	1.1	29.8
	76.363749	61%	72%	4	3.9	0.7	20.4
	114.28351	33%	81%				
	190.67626	22%	91%				
48 hours	50.765576	72%	63%	1			
	19.556624	83%	40%	2	1.6	0.2	11.4
	10.28096	94%	19%	3	5.7	1.1	29.8
	76.363749	61%	72%	4	3.9	0.7	20.4
	114.28351	33%	81%				
	190.67626	22%	91%				

FIG. 3 - 6

Prostatic Acid Phosphatase

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	6.285	10.780	6.285	10.780	6.285	10.780
average	27.111	32.250	27.111	32.250	27.111	32.250
stdev	55.574	66.832	55.574	66.832	55.574	66.832
p (t-test)		0.731		0.731		0.731
min	0.026	0.051	0.026	0.051	0.026	0.051
max	310.000	285.000	310.000	285.000	310.000	285.000
n (Samp)	54	22	54	22	54	22
n (Pat)	54	22	54	22	54	22

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	5.155	2.100	5.155	2.100	5.155	2.100
average	18.794	11.651	18.794	11.651	18.794	11.651
stdev	52.433	17.095	52.433	17.095	52.433	17.095
p (t-test)		0.770		0.770		0.770
min	0.000	0.377	0.000	0.377	0.000	0.377
max	237.000	40.600	237.000	40.600	237.000	40.600
n (Samp)	20	5	20	5	20	5
n (Pat)	20	5	20	5	20	5

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	8.005	9.360	8.005	9.360	8.005	9.360
average	27.036	38.518	27.036	38.518	27.036	38.518
stdev	51.712	75.147	51.712	75.147	51.712	75.147
p (t-test)		0.498		0.498		0.498
min	0.026	0.051	0.026	0.051	0.026	0.051
max	310.000	285.000	310.000	285.000	310.000	285.000
n (Samp)	44	17	44	17	44	17
n (Pat)	44	17	44	17	44	17

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.52	0.074	54	22	0.815
24 hours	0.52	0.074	54	22	0.815
48 hours	0.52	0.074	54	22	0.815

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.54	0.149	20	5	0.788
24 hours	0.54	0.149	20	5	0.788
48 hours	0.54	0.149	20	5	0.788

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.51	0.083	44	17	0.942
24 hours	0.51	0.083	44	17	0.942
48 hours	0.51	0.083	44	17	0.942

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	2.29	73%	31%	1			
	0.167	82%	13%	2	1.0	0.3	2.9
	0.157	91%	13%	3	1.6	0.6	4.3
	19.3	27%	70%	4	1.0	0.3	2.9
	41.8	18%	81%				
	64.9	9%	91%				

FIG. 3 - 7

24 hours	2.29	73%	31%	1			
	0.167	82%	13%	2	1.0	0.3	2.9
	0.157	91%	13%	3	1.6	0.6	4.3
	19.3	27%	70%	4	1.0	0.3	2.9
	41.8	18%	81%				
	64.9	9%	91%				
48 hours	2.29	73%	31%	1			
	0.167	82%	13%	2	1.0	0.3	2.9
	0.157	91%	13%	3	1.6	0.6	4.3
	19.3	27%	70%	4	1.0	0.3	2.9
	41.8	18%	81%				
	64.9	9%	91%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.395	80%	30%	1			
	0.395	80%	30%	2	2.5	0.1	114.2
	0.333	100%	25%	3	0.0	0.0	na
	6.92	40%	70%	4	2.0	0.0	82.9
	11.2	40%	80%				
	27.9	20%	90%				
24 hours	0.395	80%	30%	1			
	0.395	80%	30%	2	2.5	0.1	114.2
	0.333	100%	25%	3	0.0	0.0	na
	6.92	40%	70%	4	2.0	0.0	82.9
	11.2	40%	80%				
	27.9	20%	90%				
48 hours	0.395	80%	30%	1			
	0.395	80%	30%	2	2.5	0.1	114.2
	0.333	100%	25%	3	0.0	0.0	na
	6.92	40%	70%	4	2.0	0.0	82.9
	11.2	40%	80%				
	27.9	20%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	2.69	71%	34%	1			
	0.159	82%	9%	2	1.0	0.3	3.8
	0.0506	94%	7%	3	1.4	0.4	4.8
	21.6	29%	70%	4	0.9	0.2	3.4
	45.4	24%	84%				
	64.9	12%	91%				
24 hours	2.69	71%	34%	1			
	0.159	82%	9%	2	1.0	0.3	3.8
	0.0506	94%	7%	3	1.4	0.4	4.8
	21.6	29%	70%	4	0.9	0.2	3.4
	45.4	24%	84%				
	64.9	12%	91%				
48 hours	2.69	71%	34%	1			
	0.159	82%	9%	2	1.0	0.3	3.8
	0.0506	94%	7%	3	1.4	0.4	4.8
	21.6	29%	70%	4	0.9	0.2	3.4
	45.4	24%	84%				
	64.9	12%	91%				

FIG. 3 - 8

Erythropoietin receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	37.162	98.958	37.162	98.958	37.162	93.750
average	227.865	94.153	227.865	94.153	227.865	103.961
stdev	1164.013	38.050	1164.013	38.050	1164.013	42.292
p (t-test)		0.749		0.749		0.856
min	0.517	30.854	0.517	30.854	0.517	67.708
max	7307.410	150.424	7307.410	150.424	7307.410	150.424
n (Samp)	39	8	39	8	39	3
n (Pat)	39	8	39	8	39	3

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	29.785	116.702	29.785	116.702	29.785	0.517
average	143.240	103.671	143.240	103.671	143.240	150.424
stdev	857.249	52.096	857.249	52.096	857.249	na
p (t-test)		0.927		0.927		na
min	0.517	30.854	0.517	30.854	0.517	150.424
max	7307.410	150.424	7307.410	150.424	7307.410	150.424
n (Samp)	72	4	72	4	72	1
n (Pat)	72	4	72	4	72	1

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	50.366	93.750	50.366	93.750	50.366	93.750
average	284.128	97.793	284.128	97.793	284.128	103.961
stdev	1282.305	34.390	1282.305	34.390	1282.305	42.292
p (t-test)		0.750		0.750		0.812
min	0.517	67.708	0.517	67.708	0.517	67.708
max	7307.410	150.424	7307.410	150.424	7307.410	150.424
n (Samp)	32	5	32	5	32	3
n (Pat)	32	5	32	5	32	3

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.82	0.095	39	8	0.001
24 hours	0.82	0.095	39	8	0.001
48 hours	0.85	0.141	39	3	0.012

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.83	0.128	72	4	0.010
24 hours	0.83	0.128	72	4	0.010
48 hours	0.96	0.141	72	1	0.001

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.77	0.130	32	5	0.036
24 hours	0.77	0.130	32	5	0.036
48 hours	0.79	0.161	32	3	0.070

FIG. 4 - 1

Intercellular adhesion molecule 1

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	4808.185	4261.862	4808.185	4261.862	4808.185	3661.124
average	6137.573	13917.934	6137.573	13875.327	6137.573	4723.937
stdev	4688.216	27995.338	4688.216	28016.430	4688.216	3737.560
p (t-test)		0.012		0.012		0.408
min	143.975	17.651	143.975	17.651	143.975	17.651
max	20734.291	101592.853	20734.291	101592.853	20734.291	12963.420
n (Samp)	99	12	99	12	99	8
n (Pat)	99	12	99	12	99	8

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	5461.036	3544.236	5461.036	3544.236	5461.036	2238.250
average	7366.343	5789.497	7366.343	5789.497	7366.343	2009.717
stdev	8951.544	5869.092	8951.544	5869.092	8951.544	1810.865
p (t-test)		0.670		0.670		0.235
min	143.975	17.651	143.975	17.651	143.975	17.651
max	101592.853	14369.565	101592.853	14369.565	101592.853	3544.718
n (Samp)	160	6	160	6	160	4
n (Pat)	160	6	160	6	160	4

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	4546.670	4261.862	4546.670	4261.862	4546.670	4261.862
average	6015.287	17158.252	6015.287	17094.341	6015.287	5704.855
stdev	4908.163	34292.217	4908.163	34326.147	4908.163	3700.611
p (t-test)		0.006		0.006		0.880
min	143.975	1444.029	143.975	932.744	143.975	3178.457
max	20734.291	101592.853	20734.291	101592.853	20734.291	12963.420
n (Samp)	84	8	84	8	84	6
n (Pat)	84	8	84	8	84	6

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.53	0.090	99	12	0.722
24 hours	0.53	0.090	99	12	0.778
48 hours	0.43	0.101	99	8	0.492

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.41	0.112	160	6	0.433
24 hours	0.41	0.112	160	6	0.433
48 hours	0.17	0.073	160	4	0.000

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.54	0.109	84	8	0.683
24 hours	0.54	0.109	84	8	0.743
48 hours	0.54	0.125	84	6	0.775

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	3521.3941	75%	37%	1			
	3079.2743	83%	32%	2	2.1	0.4	10.6
	1296.436	92%	12%	3	1.0	0.1	8.0
	7429.533	33%	71%	4	2.1	0.4	10.6
	9387.4752	33%	81%				
	12985.454	17%	91%				

FIG. 4 - 2

24 hours	3521.3941	75%	37%	1			
	3079.2743	83%	32%	2	2.1	0.4	10.6
	878.55325	92%	4%	3	1.0	0.1	8.0
	7429.533	33%	71%	4	2.1	0.4	10.6
	9387.4752	33%	81%				
	12985.454	17%	91%				
48 hours	3521.3941	75%	37%	1			
	3079.2743	88%	32%	2	2.1	0.1	45.9
	0	100%	0%	3	4.5	0.3	61.5
	7429.533	13%	71%	4	1.0	0.0	61.1
	9387.4752	13%	81%				
	12985.454	0%	91%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	1404.7125	83%	9%	1			
	1404.7125	83%	9%	2	0.0	0.0	na
	0	100%	0%	3	1.0	0.1	7.8
	8244.2153	33%	70%	4	1.0	0.1	8.0
	10929.185	33%	80%				
	13774.777	17%	90%				
24 hours	1404.7125	83%	9%	1			
	1404.7125	83%	9%	2	0.0	0.0	na
	0	100%	0%	3	1.0	0.1	7.8
	8244.2153	33%	70%	4	1.0	0.1	8.0
	10929.185	33%	80%				
	13774.777	17%	90%				
48 hours	878.55325	75%	3%	1			
	0	100%	0%	2	na	na	na
	0	100%	0%	3	na	na	na
	8244.2153	0%	70%	4	na	na	na
	10929.185	0%	80%				
	13774.777	0%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	3521.3941	75%	40%	1			
	3079.2743	88%	37%	2	3.3	0.2	54.3
	1296.436	100%	14%	3	2.1	0.1	47.6
	6633.7291	25%	70%	4	2.1	0.1	47.6
	9553.5484	25%	81%				
	12985.454	13%	90%				
24 hours	3521.3941	75%	40%	1			
	3079.2743	88%	37%	2	3.3	0.2	54.3
	878.55325	100%	7%	3	2.1	0.1	47.6
	6633.7291	25%	70%	4	2.1	0.1	47.6
	9553.5484	25%	81%				
	12985.454	13%	90%				
48 hours	3521.3941	83%	40%	1			
	3521.3941	83%	40%	2	na	na	na
	3079.2743	100%	37%	3	na	na	na
	6633.7291	17%	70%	4	na	na	na
	9553.5484	17%	81%				
	12985.454	0%	90%				

FIG. 4 - 3

Lactotransferrin

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	44.384	159.930	44.384	159.930	44.384	116.033
average	134.659	499.716	134.659	490.326	134.659	582.143
stdev	802.709	1018.167	802.709	1020.964	802.709	1253.066
p (t-test)		0.152		0.163		0.151
min	0.034	1.565	0.034	1.565	0.034	1.565
max	7981.395	3665.116	7981.395	3665.116	7981.395	3665.116
n (Samp)	98	12	98	12	98	8
n (Pat)	98	12	98	12	98	8

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	51.326	92.341	51.326	76.923	51.326	98.231
average	168.485	110.358	168.485	105.219	168.485	106.241
stdev	705.659	104.394	705.659	105.989	705.659	92.798
p (t-test)		0.841		0.827		0.861
min	0.034	1.565	0.034	1.565	0.034	1.565
max	7981.395	308.777	7981.395	308.777	7981.395	226.935
n (Samp)	158	6	158	6	158	4
n (Pat)	158	6	158	6	158	4

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	43.062	289.569	43.062	248.648	43.062	168.190
average	168.384	718.875	168.384	708.644	168.384	761.148
stdev	893.760	1209.784	893.760	1214.085	893.760	1429.573
p (t-test)		0.110		0.117		0.136
min	0.034	23.092	0.034	23.092	0.034	23.092
max	7981.395	3665.116	7981.395	3665.116	7981.395	3665.116
n (Samp)	84	8	84	8	84	6
n (Pat)	84	8	84	8	84	6

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.79	0.081	98	12	0.000
24 hours	0.77	0.082	98	12	0.001
48 hours	0.74	0.103	98	8	0.019

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.62	0.125	158	6	0.352
24 hours	0.59	0.124	158	6	0.461
48 hours	0.60	0.152	158	4	0.525

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.89	0.077	84	8	0.000
24 hours	0.89	0.077	84	8	0.000
48 hours	0.85	0.100	84	6	0.000

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	84.873371	75%	77%	1			
	58.064804	83%	64%	2	1.0	0.0	56.3
	21.915017	92%	43%	3	2.1	0.1	45.9
	69.14188	75%	70%	4	10.4	1.0	112.2
	95.209739	67%	81%				
	118.88319	50%	91%				

FIG. 4 - 4

24 hours	63.154087	75%	67%	1			
	58.064804	83%	64%	2	1.0	0.0	56.3
	21.915017	92%	43%	3	3.3	0.2	51.9
	69.14188	67%	70%	4	8.7	0.8	96.4
	95.209739	58%	81%				
	118.88319	50%	91%				
48 hours	84.873371	75%	77%	1			
	21.915017	88%	43%	2	1.0	0.0	56.5
	1.3535835	100%	5%	3	1.0	0.0	59.0
	69.14188	75%	70%	4	5.7	0.5	70.6
	95.209739	63%	81%				
	118.88319	50%	91%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	58.662081	83%	56%	1			
	58.662081	83%	56%	2	0.0	0.0	na
	1.4945818	100%	4%	3	4.3	0.3	55.5
	94.635559	50%	70%	4	1.0	0.0	55.6
	112.67707	17%	80%				
	184.36697	17%	91%				
24 hours	58.662081	83%	56%	1			
	58.662081	83%	56%	2	0.0	0.0	na
	1.4945818	100%	4%	3	4.3	0.3	55.5
	94.635559	33%	70%	4	1.0	0.0	55.6
	112.67707	17%	80%				
	184.36697	17%	91%				
48 hours	88.510404	75%	68%	1			
	1.4945818	100%	4%	2	0.0	0.0	na
	1.4945818	100%	4%	3	2.1	0.1	43.0
	94.635559	50%	70%	4	1.0	0.0	54.3
	112.67707	25%	80%				
	184.36697	25%	91%				

FIG. 4 - 5

Prostatic Acid Phosphatase

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	9.250	18.700	9.250	14.450	9.250	17.150
average	41.398	111.095	41.398	106.876	41.398	52.031
stdev	97.909	164.515	97.909	172.062	97.909	69.731
p (t-test)		0.016		0.029		0.739
min	0.024	2.320	0.024	0.311	0.024	0.104
max	530.000	521.000	530.000	521.000	530.000	205.000
n (Samp)	103	17	103	16	103	10
n (Pat)	103	17	103	16	103	10

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	13.800	12.215	13.800	11.220	13.800	15.000
average	47.957	91.925	47.957	89.664	47.957	138.863
stdev	98.983	166.977	98.983	168.263	98.983	203.607
p (t-test)		0.238		0.263		0.053
min	0.024	4.520	0.024	0.311	0.024	0.104
max	530.000	469.000	530.000	469.000	530.000	469.000
n (Samp)	169	8	169	8	169	5
n (Pat)	169	8	169	8	169	5

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	8.880	66.600	8.880	27.150	8.880	19.300
average	31.621	147.948	31.621	146.692	31.621	42.887
stdev	81.735	189.553	81.735	202.523	81.735	51.169
p (t-test)		0.000		0.001		0.721
min	0.024	2.320	0.024	2.320	0.024	2.320
max	530.000	521.000	530.000	521.000	530.000	117.000
n (Samp)	85	11	85	10	85	7
n (Pat)	85	11	85	10	85	7

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.69	0.075	103	17	0.011
24 hours	0.61	0.080	103	16	0.160
48 hours	0.59	0.099	103	10	0.350

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.55	0.107	169	8	0.659
24 hours	0.47	0.102	169	8	0.745
48 hours	0.55	0.135	169	5	0.696

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.77	0.087	85	11	0.002
24 hours	0.72	0.095	85	10	0.018
48 hours	0.65	0.117	85	7	0.208

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	9.87	71%	52%	1			
	7.95	82%	48%	2	5.8	0.5	70.5
	4.47	94%	34%	3	3.2	0.2	50.6
	20.9	47%	71%	4	10.5	1.0	111.9
	32.9	47%	81%				
	84.7	35%	90%				

FIG. 4 - 6

24 hours	7.95	75%	48%	1			
	5.07	81%	38%	2	1.0	0.2	4.1
	0.311	94%	7%	3	1.3	0.4	4.9
	20.9	38%	71%	4	2.2	0.7	6.8
	32.9	38%	81%				
	84.7	31%	90%				
48 hours	6.27	70%	41%	1			
	5.07	80%	38%	2	1.0	0.1	8.3
	2.17	90%	21%	3	1.0	0.1	8.3
	20.9	40%	71%	4	2.1	0.4	10.6
	32.9	40%	81%				
	84.7	30%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	8.04	75%	38%	1			
	5.07	88%	31%	2	na	na	na
	4.47	100%	28%	3	na	na	na
	31.8	25%	70%	4	na	na	na
	47.5	25%	80%				
	121	25%	91%				
24 hours	5.07	75%	31%	1			
	0.311	88%	5%	2	1.0	0.1	8.0
	0.269	100%	5%	3	1.0	0.1	8.0
	31.8	25%	70%	4	1.0	0.1	8.0
	47.5	25%	80%				
	121	25%	91%				
48 hours	5.07	80%	31%	1			
	5.07	80%	31%	2	1.0	0.0	54.0
	0.0506	100%	2%	3	1.0	0.0	55.3
	31.8	40%	70%	4	2.0	0.1	41.5
	47.5	40%	80%				
	121	40%	91%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	12.1	73%	60%	1			
	9.87	82%	55%	2	1.0	0.0	59.8
	4.96	91%	39%	3	2.1	0.1	47.1
	15.7	64%	71%	4	9.5	0.8	108.7
	22.4	64%	80%				
	48.9	55%	91%				
24 hours	12.1	70%	60%	1			
	8.88	80%	51%	2	2.0	0.1	45.2
	4.96	90%	39%	3	2.0	0.1	45.2
	15.7	60%	71%	4	5.8	0.5	73.7
	22.4	50%	80%				
	48.9	40%	91%				
48 hours	6.27	71%	42%	1			
	4.96	86%	39%	2	2.1	0.1	47.6
	2.17	100%	26%	3	1.0	0.0	60.2
	15.7	57%	71%	4	3.3	0.2	54.3
	22.4	43%	80%				
	48.9	29%	91%				

FIG. 4 - 7

von Willebrand Factor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.013	0.048	0.013	0.045	0.013	0.043
average	0.055	0.880	0.055	0.924	0.055	0.193
stdev	0.236	3.017	0.236	3.111	0.236	0.488
p (t-test)		0.006		0.005		0.119
min	0.000	0.003	0.000	0.003	0.000	0.003
max	2.330	12.500	2.330	12.500	2.330	1.580
n (Samp)	103	17	103	16	103	10
n (Pat)	103	17	103	16	103	10

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.014	0.043	0.014	0.043	0.014	0.043
average	0.121	0.249	0.121	0.247	0.121	0.348
stdev	0.976	0.540	0.976	0.541	0.976	0.689
p (t-test)		0.715		0.718		0.607
min	0.000	0.003	0.000	0.003	0.000	0.003
max	12.500	1.580	12.500	1.580	12.500	1.580
n (Samp)	169	8	169	8	169	5
n (Pat)	169	8	169	8	169	5

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.013	0.058	0.013	0.053	0.013	0.043
average	0.061	1.193	0.061	1.295	0.061	0.043
stdev	0.259	3.750	0.259	3.937	0.259	0.031
p (t-test)		0.006		0.004		0.860
min	0.000	0.010	0.000	0.010	0.000	0.010
max	2.330	12.500	2.330	12.500	2.330	0.090
n (Samp)	85	11	85	10	85	7
n (Pat)	85	11	85	10	85	7

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.79	0.068	103	17	0.000
24 hours	0.76	0.072	103	16	0.000
48 hours	0.69	0.096	103	10	0.050

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.74	0.102	169	8	0.016
24 hours	0.73	0.103	169	8	0.024
48 hours	0.70	0.133	169	5	0.127

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.83	0.079	85	11	0.000
24 hours	0.80	0.087	85	10	0.001
48 hours	0.71	0.113	85	7	0.063

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.0391	71%	79%	1			
	0.0277	82%	77%	2	1.0	0.0	57.7
	0.00903	94%	45%	3	7.3	0.6	82.8
	0.0227	88%	71%	4	12.4	1.2	128.9
	0.049	47%	81%				
	0.0825	35%	90%				

FIG. 4 - 8

24 hours	0.0227	75%	71%	1			
	0.0196	81%	68%	2	1.0	0.0	55.8
	0.00903	94%	45%	3	7.0	0.6	80.2
	0.0227	75%	71%	4	10.2	1.0	108.3
	0.049	44%	81%				
	0.0825	25%	90%				
48 hours	0.0177	70%	64%	1			
	0.0113	80%	47%	2	2.1	0.1	45.6
	0.00903	90%	45%	3	1.0	0.0	58.3
	0.0227	60%	71%	4	7.0	0.6	81.2
	0.049	40%	81%				
	0.0825	20%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.0283	75%	73%	1			
	0.025	88%	67%	2	0.0	0.0	na
	0.00226	100%	9%	3	2.0	0.1	42.5
	0.0268	75%	70%	4	5.4	0.5	62.1
	0.0491	38%	80%				
	0.0882	38%	91%				
24 hours	0.0234	75%	67%	1			
	0.0207	88%	64%	2	0.0	0.0	na
	0.00226	100%	9%	3	2.0	0.1	42.5
	0.0268	63%	70%	4	5.4	0.5	62.1
	0.0491	38%	80%				
	0.0882	38%	91%				
48 hours	0.0416	80%	78%	1			
	0.0416	80%	78%	2	0.0	0.0	na
	0.00226	100%	9%	3	0.0	0.0	na
	0.0268	80%	70%	4	4.2	0.3	53.6
	0.0491	40%	80%				
	0.0882	20%	91%				

FIG. 4 - 9

Endothelial protein C receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	300.134	322.838	300.134	259.130	300.134	295.533
average	376.663	370.055	376.663	368.623	376.663	308.887
stdev	255.432	229.567	255.432	342.732	255.432	127.865
p (t-test)		0.879		0.867		0.201
min	9.942	50.726	9.942	70.603	9.942	162.252
max	1411.055	1427.189	1411.055	2040.151	1411.055	714.156
n (Samp)	103	48	103	56	103	25
n (Pat)	98	48	98	56	98	25

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	301.489	318.500	301.489	249.530	301.489	290.661
average	375.358	431.240	375.358	352.808	375.358	316.791
stdev	285.968	346.574	285.968	210.811	285.968	144.078
p (t-test)		0.456		0.731		0.482
min	9.942	50.726	9.942	106.659	9.942	127.341
max	2040.151	1427.189	2040.151	731.464	2040.151	621.974
n (Samp)	239	16	239	20	239	12
n (Pat)	159	16	159	20	159	12

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	308.294	303.794	308.294	260.000	308.294	295.533
average	384.836	320.271	384.836	365.614	384.836	313.955
stdev	250.732	140.890	250.732	365.653	250.732	149.348
p (t-test)		0.129		0.716		0.216
min	45.313	50.726	45.313	70.603	45.313	134.432
max	1411.055	621.484	1411.055	2040.151	1411.055	714.156
n (Samp)	96	40	96	45	96	21
n (Pat)	84	40	84	45	84	21

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.52	0.051	103	48	0.667
24 hours	0.44	0.047	103	56	0.219
48 hours	0.45	0.063	103	25	0.450

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.54	0.076	239	16	0.561
24 hours	0.48	0.066	239	20	0.725
48 hours	0.48	0.084	239	12	0.782

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.46	0.054	96	40	0.467
24 hours	0.42	0.050	96	45	0.102
48 hours	0.43	0.067	96	21	0.318

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	258.26667	71%	36%	1			
	218.51064	81%	24%	2	1.1	0.7	1.8
	127.34091	92%	6%	3	1.8	1.1	2.9
	422.20645	29%	71%	4	1.2	0.8	2.1
	543.48387	13%	81%				
	666.4878	4%	90%				

FIG. 5 - 1

24 hours	218.99329	71%	24%	1			
	195.43624	80%	20%	2	1.1	0.7	1.8
	150.34351	91%	11%	3	1.6	1.0	2.4
	422.20645	23%	71%	4	1.5	0.9	2.3
	543.48387	14%	81%				
	666.4878	13%	90%				
48 hours	228.21643	72%	29%	1			
	213.67021	80%	23%	2	2.3	1.0	5.7
	177.91971	92%	15%	3	2.0	0.8	4.9
	422.20645	16%	71%	4	1.6	0.6	4.2
	543.48387	4%	81%				
	666.4878	4%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	225.09018	75%	27%	1			
	220.73826	81%	26%	2	1.3	0.4	4.5
	155.70455	94%	10%	3	1.3	0.4	4.5
	401.14286	38%	71%	4	1.7	0.6	5.1
	485.6129	31%	80%				
	663.50649	13%	90%				
24 hours	228.8	70%	30%	1			
	195.43624	80%	18%	2	0.1	0.0	1.3
	124.97727	90%	6%	3	1.0	0.5	1.9
	401.14286	35%	71%	4	0.7	0.3	1.5
	485.6129	30%	80%				
	663.50649	15%	90%				
48 hours	248.73333	75%	37%	1			
	188.20455	83%	16%	2	2.1	0.4	9.6
	175.07299	92%	14%	3	1.5	0.3	8.3
	401.14286	17%	71%	4	1.6	0.3	8.5
	485.6129	17%	80%				
	663.50649	0%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	238.33333	70%	32%	1			
	213.67021	80%	22%	2	1.6	0.9	2.8
	127.34091	90%	5%	3	1.6	0.9	2.8
	437.30323	20%	71%	4	1.4	0.7	2.5
	543.48387	8%	80%				
	680.86452	0%	91%				
24 hours	219.86577	71%	24%	1			
	202.41611	80%	21%	2	1.4	0.8	2.5
	147.43182	91%	9%	3	2.6	1.5	4.5
	437.30323	18%	71%	4	1.8	1.0	3.2
	543.48387	11%	80%				
	680.86452	9%	91%				
48 hours	227.43487	71%	26%	1			
	180.85878	81%	13%	2	2.9	1.0	8.6
	172.84091	90%	13%	3	1.9	0.6	6.2
	437.30323	19%	71%	4	2.3	0.8	7.3
	543.48387	10%	80%				
	680.86452	5%	91%				

FIG. 5 - 2

Erythropoietin receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	290.373	259.902	290.373	164.120	290.373	472.159
average	1032.036	599.806	1032.036	350.893	1032.036	560.586
stdev	1811.528	684.326	1811.528	477.002	1811.528	444.842
p (t-test)		0.328		0.064		0.469
min	12.346	9.259	12.346	0.517	12.346	77.083
max	8263.287	2660.287	8263.287	1969.419	8263.287	1094.801
n (Samp)	55	18	55	26	55	8
n (Pat)	55	18	55	26	55	8

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	236.328	273.481	236.328	197.266	236.328	590.995
average	736.698	776.018	736.698	669.826	736.698	590.995
stdev	1392.724	981.406	1392.724	845.584	1392.724	570.628
p (t-test)		0.942		0.908		0.883
min	0.517	27.778	0.517	58.642	0.517	187.500
max	8263.287	2660.287	8263.287	1969.419	8263.287	994.490
n (Samp)	107	7	107	6	107	2
n (Pat)	92	7	92	6	92	2

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	395.028	246.324	395.028	154.412	395.028	236.328
average	1116.957	837.516	1116.957	593.099	1116.957	504.815
stdev	1655.909	1458.477	1655.909	1434.945	1655.909	448.490
p (t-test)		0.582		0.197		0.278
min	12.346	9.259	12.346	0.517	12.346	58.642
max	6805.195	5495.557	6805.195	6961.570	6805.195	1094.801
n (Samp)	49	13	49	23	49	9
n (Pat)	47	13	47	23	47	9

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.50	0.079	55	18	0.980
24 hours	0.34	0.062	55	26	0.011
48 hours	0.52	0.111	55	8	0.846

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.53	0.115	107	7	0.776
24 hours	0.47	0.120	107	6	0.830
48 hours	0.62	0.215	107	2	0.571

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.47	0.090	49	13	0.739
24 hours	0.34	0.066	49	23	0.013
48 hours	0.43	0.101	49	9	0.471

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	162.10938	72%	31%	1			
	158.08824	83%	31%	2	3.2	0.9	11.0
	41.666667	94%	5%	3	1.4	0.3	5.9
	548.19277	39%	71%	4	1.3	0.3	5.4
	1003.8462	22%	80%				
	4001.6353	0%	91%				
24 hours	89.583333	73%	13%	1			

FIG. 5 - 3

	77.083333	81%	11%	2	0.8	0.3	2.5
	32.407407	92%	4%	3	1.4	0.5	3.7
	548.19277	19%	71%	4	3.9	1.6	9.7
	1003.8462	8%	80%				
	4001.6353	0%	91%				
48 hours	166.01563	75%	33%	1			
	139.70588	88%	20%	2	0.9	0.1	8.8
	71.969697	100%	9%	3	0.4	0.0	10.9
	548.19277	50%	71%	4	1.5	0.2	10.4
	1003.8462	25%	80%				
	4001.6353	0%	91%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	236.32813	71%	51%	1			
	41.666667	86%	7%	2	0.0	0.0	na
	12.345679	100%	3%	3	1.6	0.3	9.3
	486.18785	43%	70%	4	1.0	0.1	7.9
	740.96386	29%	80%				
	1714.1026	14%	91%				
24 hours	77.083333	83%	11%	1			
	77.083333	83%	11%	2	0.0	0.0	na
	41.666667	100%	7%	3	1.0	0.1	8.5
	486.18785	33%	70%	4	1.0	0.1	8.5
	740.96386	33%	80%				
	1714.1026	17%	91%				
48 hours	185.54688	100%	42%	1			
	185.54688	100%	42%	2	na	na	na
	185.54688	100%	42%	3	na	na	na
	486.18785	50%	70%	4	na	na	na
	740.96386	50%	80%				
	1714.1026	0%	91%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	161.76471	77%	29%	1			
	158.08824	85%	29%	2	1.1	0.2	5.5
	132.35294	92%	16%	3	2.0	0.5	7.8
	1001.2821	23%	71%	4	0.7	0.1	4.6
	1969.419	8%	82%				
	4106.296	8%	92%				
24 hours	89.583333	74%	14%	1			
	41.666667	83%	6%	2	1.9	0.5	7.2
	32.407407	91%	4%	3	1.9	0.5	7.2
	1001.2821	9%	71%	4	6.3	1.8	21.3
	1969.419	4%	82%				
	4106.296	4%	92%				
48 hours	139.70588	78%	20%	1			
	71.969697	89%	8%	2	1.1	0.1	10.5
	41.666667	100%	6%	3	1.0	0.1	9.6
	1001.2821	22%	71%	4	1.8	0.2	12.6
	1969.419	0%	82%				
	4106.296	0%	92%				

FIG. 5 - 4

Intercellular adhesion molecule 1

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	204482.739	241775.543	204482.739	236464.429	204482.739	199424.854
average	260087.506	251803.999	260087.506	263768.024	260087.506	273925.681
stdev	170577.847	118772.456	170577.847	127195.740	170577.847	183615.648
p (t-test)		0.787		0.899		0.724
min	51907.253	77026.129	51907.253	96080.376	51907.253	74243.651
max	1060572.701	515627.792	1060572.701	557525.433	1060572.701	799828.062
n (Samp)	82	38	82	46	82	26
n (Pat)	75	38	75	46	75	26

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	205751.313	259285.036	205751.313	274982.680	205751.313	200566.044
average	249019.358	251315.582	249019.358	320208.747	249019.358	293700.982
stdev	145779.206	111831.165	145779.206	148066.411	145779.206	233747.892
p (t-test)		0.954		0.049		0.385
min	51907.253	107017.742	51907.253	131091.944	51907.253	133433.302
max	1060572.701	445880.550	1060572.701	653217.049	1060572.701	799828.062
n (Samp)	189	14	189	18	189	9
n (Pat)	129	14	129	18	129	9

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	228898.829	234819.365	228898.829	240236.907	228898.829	205637.010
average	282141.495	252614.984	282141.495	256908.914	282141.495	256146.022
stdev	151730.865	117957.093	151730.865	115893.741	151730.865	144257.263
p (t-test)		0.349		0.353		0.486
min	51907.253	77026.129	51907.253	96080.376	51907.253	74243.651
max	766357.408	515627.792	766357.408	557525.433	766357.408	621286.258
n (Samp)	74	29	74	42	74	21
n (Pat)	61	29	61	42	61	21

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.53	0.057	82	38	0.659
24 hours	0.55	0.054	82	46	0.376
48 hours	0.51	0.066	82	26	0.833

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.54	0.082	189	14	0.646
24 hours	0.67	0.073	189	18	0.023
48 hours	0.52	0.100	189	9	0.869

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.46	0.063	74	29	0.527
24 hours	0.47	0.056	74	42	0.582
48 hours	0.45	0.070	74	21	0.470

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	165000.58	71%	33%	1			
	134797.92	82%	20%	2	0.7	0.4	1.4
	114036.08	92%	10%	3	2.0	1.2	3.6
	286718.4	34%	71%	4	0.8	0.4	1.6
	384550.39	18%	80%				
	480616.58	3%	90%				

FIG. 5 - 5

24 hours	165000.58	72%	33%	1			
	145855.13	80%	24%	2	0.7	0.4	1.4
	130812.39	91%	17%	3	2.2	1.3	3.7
	286718.4	33%	71%	4	1.3	0.8	2.3
	384550.39	17%	80%				
	480616.58	9%	90%				
48 hours	147933.77	73%	26%	1			
	147365.22	81%	24%	2	1.5	0.7	3.2
	120774.31	92%	12%	3	1.0	0.4	2.3
	286718.4	31%	71%	4	1.0	0.4	2.3
	384550.39	19%	80%				
	480616.58	19%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	172340.2	71%	37%	1			
	142255.12	86%	23%	2	0.5	0.1	2.2
	120774.31	93%	12%	3	1.3	0.5	3.3
	274234.91	36%	70%	4	0.7	0.2	2.5
	356991.98	21%	80%				
	461132.6	0%	90%				
24 hours	203344.41	72%	48%	1			
	190803.13	83%	44%	2	5.3	0.5	60.6
	150701.45	94%	28%	3	4.2	0.3	52.3
	274234.91	50%	70%	4	9.1	0.9	89.7
	356991.98	33%	80%				
	461132.6	17%	90%				
48 hours	147735.92	78%	26%	1			
	133567.47	89%	20%	2	1.5	0.3	8.3
	133292.55	100%	19%	3	1.0	0.1	7.7
	274234.91	22%	70%	4	1.0	0.1	7.5
	356991.98	22%	80%				
	461132.6	22%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	165000.58	72%	24%	1			
	134797.92	83%	14%	2	2.6	1.2	5.9
	102736.37	93%	5%	3	1.3	0.5	3.1
	341114.14	21%	70%	4	2.0	0.8	4.6
	425739.15	10%	81%				
	488775.86	3%	91%				
24 hours	165000.58	71%	24%	1			
	145855.13	81%	18%	2	2.5	1.3	4.5
	130812.39	90%	12%	3	1.0	0.5	2.0
	341114.14	21%	70%	4	1.9	1.0	3.4
	425739.15	10%	81%				
	488775.86	5%	91%				
48 hours	176846.29	71%	31%	1			
	147365.22	81%	18%	2	1.7	0.6	4.6
	120851.22	90%	9%	3	1.3	0.4	3.9
	341114.14	19%	70%	4	1.8	0.6	4.9
	425739.15	14%	81%				
	488775.86	14%	91%				

FIG. 5 - 6

Lactotransferrin

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	189.238	169.432	189.238	157.709	189.238	na
average	410.560	219.736	410.560	402.839	410.560	na
stdev	475.369	146.921	475.369	447.822	475.369	na
p (t-test)		0.276		0.958		na
min	26.292	68.170	26.292	38.746	26.292	na
max	1474.768	474.937	1474.768	1361.350	1474.768	na
n (Samp)	26	8	26	17	26	0
n (Pat)	25	8	25	17	25	0

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	151.646	249.465	151.646	364.219	151.646	26.292
average	381.454	249.465	381.454	581.143	381.454	102.980
stdev	445.562	88.604	445.562	503.829	445.562	na
p (t-test)		0.680		0.234		na
min	26.292	186.813	26.292	75.132	26.292	102.980
max	1474.768	312.118	1474.768	1324.895	1474.768	102.980
n (Samp)	46	2	46	9	46	1
n (Pat)	44	2	44	9	44	1

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	237.743	152.051	237.743	118.210	237.743	26.292
average	417.246	206.539	417.246	283.252	417.246	162.964
stdev	461.939	153.486	461.939	422.509	461.939	na
p (t-test)		0.247		0.412		na
min	26.292	68.170	26.292	38.746	26.292	162.964
max	1474.768	474.937	1474.768	1361.350	1474.768	162.964
n (Samp)	27	7	27	11	27	1
n (Pat)	25	7	25	11	25	1

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.50	0.118	26	8	0.968
24 hours	0.50	0.091	26	17	0.980
48 hours	nd	nd	26	0	nd

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.63	0.217	46	2	0.549
24 hours	0.63	0.108	46	9	0.225
48 hours	0.33	0.240	46	1	0.469

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.44	0.120	27	7	0.613
24 hours	0.37	0.097	27	11	0.193
48 hours	0.41	0.276	27	1	0.737

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	99.064023	75%	38%	1			
	89.926346	88%	31%	2	1.2	0.1	15.2
	63.818697	100%	15%	3	1.8	0.2	16.4
	360.84388	25%	73%	4	0.5	0.0	16.6
	742.27848	0%	81%				
	1266.1603	0%	92%				

FIG. 5 - 7

24 hours	112.11785	71%	38%	1			
	71.650992	82%	19%	2	0.5	0.1	2.3
	38.745946	94%	4%	3	1.0	0.2	4.2
	360.84388	35%	73%	4	0.8	0.2	3.7
	742.27848	29%	81%				
	1266.1603	6%	92%				
48 hours	na	na	na	1			
	na	na	na	2	na	na	na
	na	na	na	3	na	na	na
	na	na	na	4	na	na	na
	na	na	na				
	na	na	na				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	182.77053	100%	57%	1			
	182.77053	100%	57%	2	na	na	na
	182.77053	100%	57%	3	na	na	na
	360.84388	0%	72%	4	na	na	na
	742.27848	0%	80%				
	1214.8523	0%	91%				
24 hours	152.05053	78%	52%	1			
	75.132011	89%	17%	2	0.4	0.0	11.1
	71.650992	100%	17%	3	0.9	0.1	9.2
	360.84388	56%	72%	4	2.2	0.3	13.9
	742.27848	44%	80%				
	1214.8523	11%	91%				
48 hours	99.064023	100%	33%	1			
	99.064023	100%	33%	2	na	na	na
	99.064023	100%	33%	3	na	na	na
	360.84388	0%	72%	4	na	na	na
	742.27848	0%	80%				
	1214.8523	0%	91%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	99.064023	71%	33%	1			
	89.926346	86%	30%	2	1.1	0.0	97.4
	63.818697	100%	15%	3	6.4	0.3	140.2
	360.84388	29%	70%	4	1.1	0.0	97.4
	742.27848	0%	81%				
	1266.1603	0%	93%				
24 hours	89.926346	73%	30%	1			
	42.482162	82%	11%	2	0.5	0.0	15.4
	38.745946	91%	4%	3	4.0	0.5	29.8
	360.84388	18%	70%	4	2.0	0.2	18.1
	742.27848	18%	81%				
	1266.1603	9%	93%				
48 hours	141.94526	100%	41%	1			
	141.94526	100%	41%	2	na	na	na
	141.94526	100%	41%	3	na	na	na
	360.84388	0%	70%	4	na	na	na
	742.27848	0%	81%				
	1266.1603	0%	93%				

FIG. 5 - 8

Prostatic Acid Phosphatase

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.161	0.173	0.161	0.216	0.161	0.160
average	0.445	0.241	0.445	0.489	0.445	0.215
stdev	2.973	0.298	2.973	1.226	2.973	0.217
p (t-test)		0.610		0.909		0.694
min	0.025	0.037	0.025	0.034	0.025	0.030
max	47.000	1.950	47.000	8.660	47.000	1.020
n (Samp)	255	56	255	61	255	26
n (Pat)	111	56	111	61	111	26

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.177	0.192	0.177	0.184	0.177	0.151
average	0.399	0.448	0.399	0.197	0.399	0.223
stdev	2.271	1.214	2.271	0.120	2.271	0.192
p (t-test)		0.919		0.650		0.772
min	0.025	0.041	0.025	0.034	0.025	0.088
max	47.000	5.990	47.000	0.494	47.000	0.748
n (Samp)	457	23	457	26	457	14
n (Pat)	179	23	179	26	179	14

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.165	0.182	0.165	0.223	0.165	0.180
average	0.495	0.273	0.495	0.595	0.495	0.617
stdev	3.251	0.309	3.251	1.336	3.251	1.988
p (t-test)		0.627		0.826		0.861
min	0.000	0.037	0.000	0.036	0.000	0.030
max	47.000	1.950	47.000	8.660	47.000	9.690
n (Samp)	213	51	213	53	213	23
n (Pat)	89	51	89	53	89	23

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.48	0.042	255	56	0.579
24 hours	0.56	0.042	255	61	0.152
48 hours	0.47	0.058	255	26	0.560

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.50	0.062	457	23	0.985
24 hours	0.47	0.057	457	26	0.582
48 hours	0.46	0.076	457	14	0.608

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.53	0.046	213	51	0.503
24 hours	0.59	0.045	213	53	0.042
48 hours	0.49	0.063	213	23	0.865

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.0937	71%	17%	1			
	0.0702	80%	8%	2	0.8	0.6	1.1
	0.0465	91%	2%	3	0.5	0.3	0.8
	0.218	32%	70%	4	1.2	0.9	1.6
	0.266	23%	80%				
	0.426	13%	90%				

FIG. 5 - 9

24 hours	0.118	70%	29%	1			
	0.0762	80%	11%	2	0.2	0.1	0.4
	0.0527	90%	3%	3	0.9	0.6	1.2
	0.218	48%	70%	4	1.6	1.2	2.1
	0.266	39%	80%				
	0.426	13%	90%				
48 hours	0.103	73%	25%	1			
	0.0884	81%	13%	2	1.0	0.5	2.1
	0.0697	92%	8%	3	1.2	0.6	2.3
	0.218	27%	70%	4	1.2	0.6	2.3
	0.266	19%	80%				
	0.426	8%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.122	74%	28%	1			
	0.0795	83%	13%	2	0.8	0.4	1.8
	0.0527	91%	4%	3	1.2	0.6	2.2
	0.245	35%	70%	4	0.8	0.4	1.8
	0.313	13%	80%				
	0.467	9%	90%				
24 hours	0.125	73%	29%	1			
	0.0829	81%	13%	2	1.0	0.6	1.8
	0.0742	92%	11%	3	0.7	0.3	1.4
	0.245	27%	70%	4	1.0	0.6	1.8
	0.313	19%	80%				
	0.467	4%	90%				
48 hours	0.105	71%	23%	1			
	0.0907	86%	17%	2	0.5	0.1	2.2
	0.0884	93%	15%	3	0.7	0.2	2.4
	0.245	29%	70%	4	1.3	0.5	3.2
	0.313	14%	80%				
	0.467	14%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.131	71%	34%	1			
	0.0896	80%	16%	2	0.6	0.4	1.0
	0.0568	92%	4%	3	0.8	0.5	1.2
	0.225	41%	70%	4	1.5	1.1	2.1
	0.285	29%	80%				
	0.467	14%	90%				
24 hours	0.141	72%	38%	1			
	0.0829	81%	14%	2	0.4	0.2	0.7
	0.0527	92%	3%	3	0.9	0.6	1.3
	0.225	47%	70%	4	2.0	1.4	2.7
	0.285	36%	80%				
	0.467	17%	90%				
48 hours	0.103	78%	26%	1			
	0.075	83%	11%	2	1.0	0.5	2.1
	0.0697	91%	7%	3	1.0	0.5	2.1
	0.225	30%	70%	4	0.8	0.4	1.8
	0.285	17%	80%				
	0.467	9%	90%				

FIG. 5 - 10

von Willebrand Factor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	89.500	99.100	89.500	109.000	89.500	115.000
average	97.420	107.670	97.420	121.097	97.420	114.312
stdev	36.520	39.395	36.520	50.265	36.520	43.801
p (t-test)		0.062		0.000		0.028
min	25.000	37.100	25.000	40.900	25.000	58.000
max	278.000	214.000	278.000	328.000	278.000	215.000
n (Samp)	255	56	255	61	255	26
n (Pat)	111	56	111	61	111	26

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	93.700	110.000	93.700	115.500	93.700	109.000
average	99.954	120.257	99.954	127.904	99.954	126.871
stdev	39.860	42.795	39.860	47.309	39.860	52.383
p (t-test)		0.018		0.001		0.014
min	15.600	67.200	15.600	46.500	15.600	58.000
max	328.000	217.000	328.000	239.000	328.000	224.000
n (Samp)	457	23	457	26	457	14
n (Pat)	179	23	179	26	179	14

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	90.000	99.900	90.000	106.000	90.000	115.000
average	97.479	104.239	97.479	115.174	97.479	108.109
stdev	34.231	37.463	34.231	48.825	34.231	36.605
p (t-test)		0.215		0.002		0.161
min	25.000	37.100	25.000	40.900	25.000	59.300
max	240.000	214.000	240.000	328.000	240.000	201.000
n (Samp)	213	51	213	53	213	23
n (Pat)	89	51	89	53	89	23

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.59	0.043	255	56	0.029
24 hours	0.66	0.041	255	61	0.000
48 hours	0.61	0.061	255	26	0.068

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.65	0.064	457	23	0.019
24 hours	0.68	0.059	457	26	0.002
48 hours	0.65	0.081	457	14	0.057

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.57	0.046	213	51	0.142
24 hours	0.62	0.045	213	53	0.007
48 hours	0.59	0.065	213	23	0.176

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	88	71%	49%	1			
	83.8	80%	43%	2	1.4	0.9	2.1
	66.8	91%	16%	3	2.6	1.8	3.8
	106	45%	70%	4	1.8	1.2	2.7
	122	23%	80%				
	143	20%	90%				

FIG. 5 - 11

24 hours	96.2	70%	59%	1			
	81.4	80%	37%	2	1.1	0.7	1.9
	69.9	90%	21%	3	3.4	2.3	5.1
	106	52%	70%	4	3.4	2.3	5.1
	122	31%	80%				
	143	21%	90%				
48 hours	81.3	73%	37%	1			
	72.3	81%	25%	2	0.5	0.2	1.4
	62.3	92%	11%	3	1.0	0.5	2.0
	106	58%	70%	4	2.0	1.1	3.5
	122	35%	80%				
	143	19%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	91.8	74%	48%	1			
	90	83%	46%	2	3.7	1.0	13.3
	84.6	91%	39%	3	2.6	0.6	10.5
	112	48%	72%	4	4.8	1.4	16.4
	123	30%	80%				
	149	26%	90%				
24 hours	100	73%	59%	1			
	76.8	85%	30%	2	1.3	0.4	4.3
	66.5	92%	17%	3	2.4	0.9	6.3
	112	62%	72%	4	4.3	1.8	10.1
	123	46%	80%				
	149	35%	90%				
48 hours	96.3	71%	54%	1			
	86	86%	41%	2	1.0	0.1	7.3
	70.4	93%	21%	3	2.5	0.6	10.4
	112	50%	72%	4	2.5	0.6	10.4
	123	36%	80%				
	149	36%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	86.4	71%	44%	1			
	75.7	80%	29%	2	1.1	0.7	1.7
	64.5	90%	13%	3	1.8	1.2	2.7
	107	41%	71%	4	1.5	1.0	2.3
	122	22%	80%				
	147	10%	90%				
24 hours	93.4	72%	55%	1			
	81.3	81%	36%	2	0.7	0.4	1.3
	68.8	91%	19%	3	2.8	1.9	4.1
	107	47%	71%	4	2.2	1.4	3.2
	122	25%	80%				
	147	13%	90%				
48 hours	75.2	74%	29%	1			
	68.5	83%	19%	2	0.3	0.1	1.2
	63.6	91%	12%	3	0.8	0.4	1.8
	107	61%	71%	4	1.8	1.0	3.3
	122	26%	80%				
	147	9%	90%				

FIG. 5 - 12

Endothelial protein C receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	307.167	264.840	307.167	260.000	307.167	272.911
average	363.211	318.003	363.211	357.369	363.211	451.633
stdev	219.064	223.825	219.064	414.446	219.064	411.063
p (t-test)		0.389		0.905		0.148
min	9.942	160.019	9.942	18.516	9.942	134.432
max	1427.189	1169.184	1427.189	2040.151	1427.189	1647.301
n (Samp)	230	19	230	29	230	16
n (Pat)	158	19	158	29	158	16

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	301.977	231.676	301.977	261.383	301.977	222.660
average	377.797	231.676	377.797	363.566	377.797	302.452
stdev	276.515	101.338	276.515	272.984	276.515	221.117
p (t-test)		0.456		0.893		0.545
min	9.942	160.019	9.942	106.659	9.942	175.649
max	2040.151	303.333	2040.151	787.839	2040.151	695.922
n (Samp)	294	2	294	7	294	5
n (Pat)	186	2	186	7	186	5

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	309.594	264.840	309.594	239.670	309.594	272.911
average	360.149	330.437	360.149	326.661	360.149	451.866
stdev	207.033	227.949	207.033	415.884	207.033	430.967
p (t-test)		0.554		0.499		0.146
min	45.313	160.763	45.313	18.516	45.313	134.432
max	1411.055	1169.184	1411.055	2040.151	1411.055	1647.301
n (Samp)	198	19	198	27	198	14
n (Pat)	132	19	132	27	132	14

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.40	0.064	230	19	0.128
24 hours	0.38	0.051	230	29	0.019
48 hours	0.48	0.074	230	16	0.781

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.30	0.158	294	2	0.212
24 hours	0.46	0.107	294	7	0.709
48 hours	0.34	0.109	294	5	0.151

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.42	0.065	198	19	0.235
24 hours	0.34	0.050	198	27	0.001
48 hours	0.47	0.079	198	14	0.725

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	232.95302	74%	27%	1			
	184.65909	84%	12%	2	3.3	0.8	12.9
	160.01908	95%	8%	3	3.3	0.8	12.9
	409.24675	11%	70%	4	2.7	0.6	11.3
	503.06003	11%	80%				
	607.39355	5%	90%				

FIG. 6 - 1

24 hours	124.97727	76%	4%	1			
	108.43182	83%	3%	2	0.6	0.3	1.6
	71.368243	93%	2%	3	1.2	0.6	2.3
	409.24675	21%	70%	4	2.3	1.3	4.0
	503.06003	14%	80%				
	607.39355	14%	90%				
48 hours	175.64885	75%	10%	1			
	172.84091	81%	10%	2	0.3	0.1	1.3
	151.56818	94%	8%	3	0.0	0.0	na
	409.24675	44%	70%	4	1.4	0.7	2.7
	503.06003	25%	80%				
	607.39355	25%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	155.70455	100%	10%	1			
	155.70455	100%	10%	2	na	na	na
	155.70455	100%	10%	3	na	na	na
	409.24675	0%	70%	4	na	na	na
	514.5974	0%	80%				
	638.59355	0%	90%				
24 hours	239.6696	71%	31%	1			
	124.97727	86%	5%	2	0.5	0.0	10.0
	101.34091	100%	4%	3	1.0	0.1	7.6
	409.24675	29%	70%	4	1.0	0.1	7.6
	514.5974	29%	80%				
	638.59355	29%	90%				
48 hours	188.20455	80%	15%	1			
	188.20455	80%	15%	2	0.0	0.0	na
	175.07299	100%	13%	3	1.0	0.0	53.1
	409.24675	20%	70%	4	3.1	0.2	45.0
	514.5974	20%	80%				
	638.59355	20%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	231.20805	74%	28%	1			
	184.65909	84%	12%	2	1.4	0.4	4.7
	172.84091	95%	11%	3	2.6	0.9	7.1
	409.24675	16%	70%	4	1.8	0.6	5.4
	503.06003	16%	80%				
	611.95122	5%	90%				
24 hours	124.97727	70%	4%	1			
	95.962838	81%	3%	2	1.0	0.4	2.9
	71.368243	93%	2%	3	1.9	0.8	4.4
	409.24675	15%	70%	4	3.6	1.7	7.5
	503.06003	7%	80%				
	611.95122	7%	90%				
48 hours	172.84091	71%	11%	1			
	155.70455	86%	8%	2	0.4	0.1	1.6
	150.38636	93%	8%	3	0.0	0.0	na
	409.24675	43%	70%	4	1.5	0.7	3.1
	503.06003	21%	80%				
	611.95122	21%	90%				

FIG. 6 - 2

Erythropoietin receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	274.862	na	274.862	156.882	274.862	135.398
average	901.480	na	901.480	431.324	901.480	137.301
stdev	1563.579	na	1563.579	963.525	1563.579	39.498
p (t-test)		na		0.275		0.332
min	0.517	na	0.517	0.517	0.517	90.909
max	8263.287	na	8263.287	3753.930	8263.287	187.500
n (Samp)	112	0	112	14	112	4
n (Pat)	93	0	93	14	93	4

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	256.211	na	256.211	205.078	256.211	123.071
average	866.276	na	866.276	199.947	866.276	123.071
stdev	1522.392	na	1522.392	117.920	1522.392	91.116
p (t-test)		na		0.452		0.493
min	0.517	na	0.517	79.545	0.517	58.642
max	8263.287	na	8263.287	315.217	8263.287	187.500
n (Samp)	127	0	127	3	127	2
n (Pat)	106	0	106	3	106	2

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	290.373	na	290.373	136.029	290.373	134.766
average	908.788	na	908.788	494.427	908.788	120.568
stdev	1493.466	na	1493.466	1087.967	1493.466	25.693
p (t-test)		na		0.375		0.365
min	0.517	na	0.517	0.517	0.517	90.909
max	6961.570	na	6961.570	3753.930	6961.570	136.029
n (Samp)	95	0	95	11	95	3
n (Pat)	78	0	78	11	78	3

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	nd	nd	112	0	nd
24 hours	0.32	0.068	112	14	0.008
48 hours	0.21	0.090	112	4	0.001

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	nd	nd	127	0	nd
24 hours	0.36	0.146	127	3	0.341
48 hours	0.23	0.132	127	2	0.041

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	nd	nd	95	0	nd
24 hours	0.32	0.076	95	11	0.017
48 hours	0.18	0.092	95	3	0.001

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	na	na	na	1			
	na	na	na	2	na	na	na
	na	na	na	3	na	na	na
	na	na	na	4	na	na	na
	na	na	na				
	na	na	na				
24 hours	114.58333	71%	15%	1			

FIG. 6 - 3

	77.083333	86%	13%	2	3.3	0.2	51.8
	41.666667	93%	7%	3	3.2	0.2	49.9
	663.91185	7%	71%	4	9.0	0.8	98.2
	1006.1162	7%	80%				
	2121.6678	7%	90%				
48 hours	132.35294	75%	18%	1			
	83.333333	100%	14%	2	na	na	na
	83.333333	100%	14%	3	na	na	na
	663.91185	0%	71%	4	na	na	na
	1006.1162	0%	80%				
	2121.6678	0%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	na	na	na	1			
	na	na	na	2	na	na	na
	na	na	na	3	na	na	na
	na	na	na	4	na	na	na
	na	na	na				
	na	na	na				
24 hours	114.58333	73%	17%	1			
	97.916667	82%	17%	2	2.2	0.1	48.0
	41.666667	91%	8%	3	2.1	0.1	45.9
	707.98898	9%	71%	4	7.8	0.7	91.3
	1045.8716	9%	80%				
	2611.6108	9%	91%				
48 hours	83.333333	100%	16%	1			
	83.333333	100%	16%	2	na	na	na
	83.333333	100%	16%	3	na	na	na
	707.98898	0%	71%	4	na	na	na
	1045.8716	0%	80%				
	2611.6108	0%	91%				

FIG. 6 - 4

Intercellular adhesion molecule 1

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	212720.282	195987.185	212720.282	204249.960	212720.282	196393.305
average	258888.313	270628.556	258888.313	243905.418	258888.313	261418.055
stdev	149719.996	161880.148	149719.996	111904.661	149719.996	176673.663
p (t-test)		0.839		0.643		0.948
min	51907.253	121487.749	51907.253	98212.086	51907.253	122320.133
max	1060572.701	482503.909	1060572.701	515627.792	1060572.701	807280.039
n (Samp)	192	7	192	23	192	17
n (Pat)	129	7	129	23	129	17

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	210350.573	143846.960	210350.573	245214.865	210350.573	221188.854
average	255004.781	204460.199	255004.781	322814.481	255004.781	313388.160
stdev	143929.862	124850.396	143929.862	183649.684	143929.862	251599.617
p (t-test)		0.546		0.224		0.338
min	51907.253	121487.749	51907.253	152881.538	51907.253	147933.768
max	1060572.701	348045.889	1060572.701	653217.049	1060572.701	807280.039
n (Samp)	235	3	235	7	235	6
n (Pat)	154	3	154	7	154	6

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	223529.275	335646.849	223529.275	209260.645	223529.275	252584.630
average	266850.987	320254.823	266850.987	243022.810	266850.987	253861.700
stdev	146387.464	185355.542	146387.464	107601.465	146387.464	126267.316
p (t-test)		0.474		0.493		0.756
min	51907.253	127221.684	51907.253	98212.086	51907.253	122320.133
max	799828.062	482503.909	799828.062	515627.792	799828.062	557525.433
n (Samp)	165	4	165	19	165	13
n (Pat)	106	4	106	19	106	13

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.50	0.111	192	7	0.989
24 hours	0.50	0.064	192	23	0.997
48 hours	0.49	0.073	192	17	0.891

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.37	0.147	235	3	0.389
24 hours	0.62	0.115	235	7	0.309
48 hours	0.55	0.123	235	6	0.679

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.58	0.151	165	4	0.610
24 hours	0.48	0.069	165	19	0.752
48 hours	0.48	0.083	165	13	0.841

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	142881.92	71%	22%	1			
	126735.51	86%	14%	2	0.0	0.0	na
	120851.22	100%	11%	3	0.3	0.0	4.7
	301522.93	43%	70%	4	1.0	0.3	4.1
	377720.11	29%	80%				
	461132.6	29%	90%				

FIG. 6 - 5

24 hours	171458.56	74%	35%	1			
	150701.45	83%	28%	2	1.2	0.6	2.7
	133433.3	91%	18%	3	1.7	0.8	3.5
	301522.93	26%	70%	4	0.8	0.3	2.1
	377720.11	17%	80%				
	461132.6	4%	90%				
48 hours	150701.45	71%	28%	1			
	147735.92	82%	27%	2	1.8	0.6	5.5
	126735.51	94%	14%	3	2.2	0.8	6.3
	301522.93	24%	70%	4	1.0	0.3	4.1
	377720.11	12%	80%				
	461132.6	12%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	120851.22	100%	11%	1			
	120851.22	100%	11%	2	0.0	0.0	na
	120851.22	100%	11%	3	0.0	0.0	na
	288238.02	33%	70%	4	2.1	0.1	41.9
	363338.73	0%	80%				
	461132.6	0%	90%				
24 hours	190803.13	71%	42%	1			
	172617.78	86%	35%	2	na	na	na
	150701.45	100%	28%	3	na	na	na
	288238.02	43%	70%	4	na	na	na
	363338.73	43%	80%				
	461132.6	14%	90%				
48 hours	147933.77	83%	27%	1			
	147933.77	83%	27%	2	na	na	na
	147735.92	100%	26%	3	na	na	na
	288238.02	33%	70%	4	na	na	na
	363338.73	17%	80%				
	461132.6	17%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	195907.81	75%	37%	1			
	126735.51	100%	12%	2	1.0	0.0	55.5
	126735.51	100%	12%	3	0.0	0.0	na
	308717.07	50%	70%	4	2.0	0.1	41.6
	377720.11	50%	80%				
	474692.34	50%	90%				
24 hours	171458.56	74%	30%	1			
	146350.44	84%	19%	2	2.2	0.7	6.3
	132077.56	95%	14%	3	1.7	0.6	5.5
	308717.07	26%	70%	4	1.7	0.6	5.5
	377720.11	11%	80%				
	474692.34	5%	90%				
48 hours	150554.2	77%	23%	1			
	132077.56	85%	14%	2	1.4	0.4	4.8
	126735.51	92%	12%	3	0.7	0.1	3.7
	308717.07	23%	70%	4	1.4	0.4	4.8
	377720.11	15%	80%				
	474692.34	8%	90%				

FIG. 6 - 6

Lactotransferrin

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	198.131	na	198.131	111.248	198.131	26.292
average	404.005	na	404.005	342.527	404.005	162.964
stdev	442.278	na	442.278	407.022	442.278	na
p (t-test)		na		0.655		na
min	26.292	na	26.292	61.643	26.292	162.964
max	1474.768	na	1474.768	1168.270	1474.768	162.964
n (Samp)	46	0	46	13	46	1
n (Pat)	43	0	43	13	43	1

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	175.697	na	175.697	76.002	175.697	na
average	385.110	na	385.110	492.010	385.110	na
stdev	430.316	na	430.316	721.300	430.316	na
p (t-test)		na		0.685		na
min	26.292	na	26.292	75.132	26.292	na
max	1474.768	na	1474.768	1324.895	1474.768	na
n (Samp)	58	0	58	3	58	0
n (Pat)	54	0	54	3	54	0

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	191.259	na	191.259	111.248	191.259	26.292
average	377.491	na	377.491	344.903	377.491	162.964
stdev	436.242	na	436.242	405.417	436.242	na
p (t-test)		na		0.813		na
min	26.292	na	26.292	61.643	26.292	162.964
max	1474.768	na	1474.768	1168.270	1474.768	162.964
n (Samp)	40	0	40	13	40	1
n (Pat)	37	0	37	13	37	1

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	nd	nd	46	0	nd
24 hours	0.43	0.088	46	13	0.430
48 hours	0.43	0.280	46	1	0.816

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	nd	nd	58	0	nd
24 hours	0.42	0.161	58	3	0.618
48 hours	nd	nd	58	0	nd

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	nd	nd	40	0	nd
24 hours	0.46	0.091	40	13	0.643
48 hours	0.45	0.285	40	1	0.861

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	na	na	na	1			
	na	na	na	2	na	na	na
	na	na	na	3	na	na	na
	na	na	na	4	na	na	na
	na	na	na				
	na	na	na				

FIG. 6 - 7

24 hours	90.361473	77%	24%	1			
	89.926346	85%	24%	2	0.3	0.0	5.3
	71.650992	92%	17%	3	2.7	0.7	10.4
	362.19409	31%	72%	4	1.1	0.2	5.7
	763.88186	23%	80%				
	1214.8523	0%	91%				
48 hours	157.70947	100%	43%	1			
	157.70947	100%	43%	2	na	na	na
	157.70947	100%	43%	3	na	na	na
	362.19409	0%	72%	4	na	na	na
	763.88186	0%	80%				
	1214.8523	0%	91%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	na	na	na	1			
	na	na	na	2	na	na	na
	na	na	na	3	na	na	na
	na	na	na	4	na	na	na
	na	na	na				
	na	na	na				
24 hours	71.650992	100%	16%	1			
	71.650992	100%	16%	2	0.0	0.0	na
	71.650992	100%	16%	3	0.0	0.0	na
	360.84388	33%	71%	4	2.3	0.1	57.8
	763.88186	33%	81%				
	1168.27	33%	91%				
48 hours	na	na	na	1			
	na	na	na	2	na	na	na
	na	na	na	3	na	na	na
	na	na	na	4	na	na	na
	na	na	na				
	na	na	na				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	na	na	na	1			
	na	na	na	2	na	na	na
	na	na	na	3	na	na	na
	na	na	na	4	na	na	na
	na	na	na				
	na	na	na				
24 hours	94.27762	77%	28%	1			
	90.361473	85%	28%	2	0.2	0.0	3.5
	89.926346	92%	28%	3	2.1	0.6	7.8
	312.11789	31%	70%	4	0.5	0.1	2.9
	666.66667	23%	80%				
	1214.8523	0%	90%				
48 hours	152.05053	100%	45%	1			
	152.05053	100%	45%	2	na	na	na
	152.05053	100%	45%	3	na	na	na
	312.11789	0%	70%	4	na	na	na
	666.66667	0%	80%				
	1214.8523	0%	90%				

FIG. 6 - 8

Prostatic Acid Phosphatase

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.167	0.184	0.167	0.247	0.167	0.252
average	0.383	0.460	0.383	0.404	0.383	0.950
stdev	2.325	1.108	2.325	0.456	2.325	2.303
p (t-test)		0.861		0.955		0.310
min	0.000	0.047	0.000	0.036	0.000	0.030
max	47.000	5.990	47.000	2.510	47.000	9.690
n (Samp)	434	28	434	36	434	18
n (Pat)	173	28	173	36	173	18

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.174	0.412	0.174	0.210	0.174	0.192
average	0.388	1.269	0.388	0.453	0.388	0.198
stdev	2.126	2.317	2.126	0.733	2.126	0.116
p (t-test)		0.313		0.923		0.814
min	0.000	0.080	0.000	0.084	0.000	0.076
max	47.000	5.990	47.000	2.510	47.000	0.384
n (Samp)	542	6	542	10	542	7
n (Pat)	208	6	208	10	208	7

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.167	0.173	0.167	0.278	0.167	0.280
average	0.420	0.264	0.420	0.487	0.420	1.542
stdev	2.565	0.252	2.565	0.737	2.565	2.711
p (t-test)		0.753		0.882		0.089
min	0.000	0.047	0.000	0.036	0.000	0.030
max	47.000	1.180	47.000	4.210	47.000	9.690
n (Samp)	356	27	356	32	356	16
n (Pat)	138	27	138	32	138	16

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.56	0.058	434	28	0.315
24 hours	0.65	0.051	434	36	0.003
48 hours	0.63	0.072	434	18	0.067

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.75	0.116	542	6	0.029
24 hours	0.59	0.095	542	10	0.364
48 hours	0.49	0.109	542	7	0.951

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.54	0.059	356	27	0.535
24 hours	0.68	0.054	356	32	0.001
48 hours	0.68	0.075	356	16	0.017

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.14	71%	36%	1			
	0.0896	82%	18%	2	1.0	0.5	2.0
	0.0568	93%	6%	3	0.8	0.4	1.8
	0.224	43%	70%	4	1.9	1.1	3.3
	0.283	36%	80%				
	0.409	18%	90%				

FIG. 6 - 9

24 hours	0.16	72%	48%	1			
	0.141	81%	38%	2	0.8	0.4	1.7
	0.0751	92%	13%	3	1.4	0.7	2.5
	0.224	61%	70%	4	3.1	1.9	5.0
	0.283	42%	80%				
	0.409	28%	90%				
48 hours	0.191	72%	58%	1			
	0.118	83%	29%	2	0.7	0.1	3.5
	0.041	94%	2%	3	1.3	0.4	4.4
	0.224	56%	70%	4	3.2	1.3	7.9
	0.283	39%	80%				
	0.409	17%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.262	83%	74%	1			
	0.262	83%	74%	2	0.0	0.0	na
	0.0795	100%	14%	3	1.0	0.0	51.9
	0.243	83%	70%	4	4.1	0.3	48.8
	0.313	67%	80%				
	0.465	17%	90%				
24 hours	0.181	70%	51%	1			
	0.126	80%	29%	2	0.5	0.0	9.7
	0.0964	90%	20%	3	2.0	0.5	9.1
	0.243	40%	70%	4	1.5	0.3	8.0
	0.313	30%	80%				
	0.465	20%	90%				
48 hours	0.105	71%	24%	1			
	0.0884	86%	16%	2	1.0	0.1	7.4
	0.0751	100%	13%	3	0.0	0.0	na
	0.243	43%	70%	4	1.5	0.3	8.0
	0.313	14%	80%				
	0.465	0%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.14	70%	37%	1			
	0.0896	81%	18%	2	1.0	0.5	2.0
	0.0568	93%	6%	3	1.0	0.5	2.0
	0.225	41%	70%	4	1.5	0.9	2.8
	0.283	30%	80%				
	0.409	15%	90%				
24 hours	0.204	72%	63%	1			
	0.149	81%	42%	2	0.8	0.3	2.0
	0.0751	91%	13%	3	1.2	0.6	2.6
	0.225	63%	70%	4	3.9	2.2	6.8
	0.283	47%	80%				
	0.409	31%	90%				
48 hours	0.196	75%	61%	1			
	0.131	81%	34%	2	1.0	0.1	7.4
	0.041	94%	2%	3	1.5	0.3	8.1
	0.225	63%	70%	4	4.9	1.4	16.9
	0.283	50%	80%				
	0.409	31%	90%				

FIG. 6 - 10

von Willebrand Factor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	93.350	98.950	93.350	106.000	93.350	114.000
average	99.462	107.729	99.462	124.542	99.462	113.367
stdev	36.124	40.861	36.124	63.075	36.124	48.944
p (t-test)		0.245		0.000		0.116
min	25.000	36.800	25.000	34.300	25.000	15.600
max	278.000	195.000	278.000	328.000	278.000	201.000
n (Samp)	434	28	434	36	434	18
n (Pat)	173	28	173	36	173	18

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	93.350	117.500	93.350	161.000	93.350	143.000
average	100.001	121.850	100.001	145.500	100.001	136.257
stdev	39.553	26.303	39.553	41.513	39.553	43.024
p (t-test)		0.178		0.000		0.016
min	15.600	94.100	15.600	59.600	15.600	83.800
max	328.000	166.000	328.000	195.000	328.000	194.000
n (Samp)	542	6	542	10	542	7
n (Pat)	208	6	208	10	208	7

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	93.900	97.900	93.900	98.650	93.900	105.500
average	98.210	107.078	98.210	121.256	98.210	109.269
stdev	33.015	41.446	33.015	64.423	33.015	49.003
p (t-test)		0.188		0.001		0.201
min	25.000	36.800	25.000	34.300	25.000	15.600
max	240.000	195.000	240.000	328.000	240.000	201.000
n (Samp)	356	27	356	32	356	16
n (Pat)	138	27	138	32	138	16

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.57	0.058	434	28	0.235
24 hours	0.60	0.052	434	36	0.045
48 hours	0.60	0.072	434	18	0.149

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.73	0.118	542	6	0.051
24 hours	0.80	0.085	542	10	0.001
48 hours	0.74	0.108	542	7	0.023

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.56	0.059	356	27	0.287
24 hours	0.58	0.055	356	32	0.136
48 hours	0.58	0.076	356	16	0.277

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	90.5	71%	47%	1			
	76.3	82%	29%	2	1.8	0.8	4.0
	58.5	93%	8%	3	2.1	1.0	4.5
	112	32%	71%	4	2.3	1.1	4.9
	123	25%	80%				
	148	18%	90%				

FIG. 6 - 11

24 hours	85.4	72%	40%	1			
	71.7	81%	22%	2	0.7	0.4	1.3
	60.9	92%	9%	3	0.9	0.5	1.5
	112	47%	71%	4	2.0	1.3	3.0
	123	39%	80%				
	148	28%	90%				
48 hours	86.9	72%	41%	1			
	73	83%	24%	2	0.7	0.2	2.4
	47	94%	3%	3	0.5	0.1	2.2
	112	50%	71%	4	2.4	1.1	5.0
	123	39%	80%				
	148	22%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	99.9	83%	58%	1			
	99.9	83%	58%	2	na	na	na
	93.7	100%	51%	3	na	na	na
	112	67%	71%	4	na	na	na
	123	33%	80%				
	149	17%	90%				
24 hours	142	70%	88%	1			
	124	80%	81%	2	0.0	0.0	na
	94.3	90%	51%	3	1.0	0.0	51.9
	112	80%	71%	4	8.4	0.9	78.7
	123	80%	80%				
	149	60%	90%				
48 hours	109	71%	68%	1			
	87.9	86%	43%	2	na	na	na
	83.5	100%	37%	3	na	na	na
	112	57%	71%	4	na	na	na
	123	57%	80%				
	149	43%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	87.7	70%	42%	1			
	75.8	81%	28%	2	1.4	0.7	2.9
	58.5	93%	8%	3	1.4	0.7	2.9
	111	33%	71%	4	1.6	0.8	3.2
	121	26%	81%				
	145	19%	90%				
24 hours	85.4	72%	40%	1			
	71.6	81%	21%	2	1.0	0.5	1.8
	63.6	91%	12%	3	0.7	0.3	1.4
	111	41%	71%	4	2.0	1.2	3.2
	121	31%	81%				
	145	22%	90%				
48 hours	86.9	75%	40%	1			
	73	81%	22%	2	0.5	0.1	2.2
	47	94%	3%	3	0.7	0.2	2.4
	111	44%	71%	4	1.8	0.8	4.1
	121	38%	81%				
	145	19%	90%				

FIG. 6 - 12

Endothelial protein C receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	348.048	246.289	348.048	246.289	348.048	246.289
average	388.855	259.168	388.855	259.168	388.855	259.168
stdev	224.593	172.646	224.593	172.646	224.593	172.646
p (t-test)		0.038		0.038		0.038
min	50.726	18.516	50.726	18.516	50.726	18.516
max	1427.189	575.377	1427.189	575.377	1427.189	575.377
n						
(Samp)	52	16	52	16	52	16
n (Pat)	52	16	52	16	52	16

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	324.133	242.021	324.133	242.021	324.133	242.021
average	431.867	242.021	431.867	242.021	431.867	242.021
stdev	320.686	27.382	320.686	27.382	320.686	27.382
p (t-test)		0.423		0.423		0.423
min	50.726	222.660	50.726	222.660	50.726	222.660
max	1427.189	261.383	1427.189	261.383	1427.189	261.383
n						
(Samp)	19	2	19	2	19	2
n (Pat)	19	2	19	2	19	2

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	343.612	218.056	343.612	218.056	343.612	218.056
average	350.231	238.936	350.231	238.936	350.231	238.936
stdev	152.796	162.756	152.796	162.756	152.796	162.756
p (t-test)		0.028		0.028		0.028
min	50.726	18.516	50.726	18.516	50.726	18.516
max	754.335	492.312	754.335	492.312	754.335	492.312
n						
(Samp)	41	13	41	13	41	13
n (Pat)	41	13	41	13	41	13

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.31	0.071	52	16	0.009
24 hours	0.31	0.071	52	16	0.009
48 hours	0.31	0.071	52	16	0.009

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.21	0.141	19	2	0.041
24 hours	0.21	0.141	19	2	0.041
48 hours	0.21	0.141	19	2	0.041

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.30	0.078	41	13	0.012
24 hours	0.30	0.078	41	13	0.012
48 hours	0.30	0.078	41	13	0.012

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	109.61364	75%	4%	1			
	101.34091	81%	4%	2	0.6	0.1	4.2
	71.368243	94%	4%	3	1.0	0.2	4.9
	426.46753	25%	71%	4	4.1	1.2	14.6

FIG. 7 - 1

	514.5974	6%	81%				
	607.39355	0%	90%				
24 hours	109.61364	75%	4%	1			
	101.34091	81%	4%	2	0.6	0.1	4.2
	71.368243	94%	4%	3	1.0	0.2	4.9
	426.46753	25%	71%	4	4.1	1.2	14.6
	514.5974	6%	81%				
	607.39355	0%	90%				
48 hours	109.61364	75%	4%	1			
	101.34091	81%	4%	2	0.6	0.1	4.2
	71.368243	94%	4%	3	1.0	0.2	4.9
	426.46753	25%	71%	4	4.1	1.2	14.6
	514.5974	6%	81%				
	607.39355	0%	90%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	101.34091	77%	5%	1			
	77.077703	85%	5%	2	0.3	0.0	5.9
	71.368243	92%	5%	3	1.0	0.2	5.3
	417.35065	23%	71%	4	3.1	0.7	13.2
	482.58537	8%	80%				
	544.98701	0%	93%				
24 hours	101.34091	77%	5%	1			
	77.077703	85%	5%	2	0.3	0.0	5.9
	71.368243	92%	5%	3	1.0	0.2	5.3
	417.35065	23%	71%	4	3.1	0.7	13.2
	482.58537	8%	80%				
	544.98701	0%	93%				
48 hours	101.34091	77%	5%	1			
	77.077703	85%	5%	2	0.3	0.0	5.9
	71.368243	92%	5%	3	1.0	0.2	5.3
	417.35065	23%	71%	4	3.1	0.7	13.2
	482.58537	8%	80%				
	544.98701	0%	93%				

FIG. 7 - 2

Erythropoietin receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	242.647	254.240	242.647	254.240	242.647	254.240
average	838.906	1290.891	838.906	1290.891	838.906	1290.891
stdev	1460.675	1710.982	1460.675	1710.982	1460.675	1710.982
p (t-test)		0.517		0.517		0.517
min	9.259	126.953	9.259	126.953	9.259	126.953
max	6961.570	3753.930	6961.570	3753.930	6961.570	3753.930
n (Samp)	24	6	24	6	24	6
n (Pat)	24	6	24	6	24	6

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	450.790	na	450.790	na	450.790	na
average	1569.698	na	1569.698	na	1569.698	na
stdev	2215.935	na	2215.935	na	2215.935	na
p (t-test)		na		na		na
min	27.778	na	27.778	na	27.778	na
max	6961.570	na	6961.570	na	6961.570	na
n (Samp)	10	0	10	0	10	0
n (Pat)	10	0	10	0	10	0

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	236.328	177.734	236.328	177.734	236.328	177.734
average	775.297	905.079	775.297	905.079	775.297	905.079
stdev	1310.562	1594.660	1310.562	1594.660	1310.562	1594.660
p (t-test)		0.854		0.854		0.854
min	9.259	126.953	9.259	126.953	9.259	126.953
max	5495.557	3753.930	5495.557	3753.930	5495.557	3753.930
n (Samp)	17	5	17	5	17	5
n (Pat)	17	5	17	5	17	5

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.53	0.135	24	6	0.837
24 hours	0.53	0.135	24	6	0.837
48 hours	0.53	0.135	24	6	0.837

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	nd	nd	10	0	nd
24 hours	nd	nd	10	0	nd
48 hours	nd	nd	10	0	nd

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.42	0.144	17	5	0.595
24 hours	0.42	0.144	17	5	0.595
48 hours	0.42	0.144	17	5	0.595

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	126.95313	83%	17%	1			
	126.95313	83%	17%	2	0.4	0.0	13.2
	125	100%	17%	3	0.4	0.0	16.2
	634.93976	33%	71%	4	0.8	0.1	12.1
	1406.7278	33%	83%				
	1714.1026	33%	92%				
24 hours	126.95313	83%	17%	1			

FIG. 7 - 3

	126.95313	83%	17%	2	0.4	0.0	13.2
	125	100%	17%	3	0.4	0.0	16.2
	634.93976	33%	71%	4	0.8	0.1	12.1
	1406.7278	33%	83%				
	1714.1026	33%	92%				
48 hours	126.95313	83%	17%	1			
	126.95313	83%	17%	2	0.4	0.0	13.2
	125	100%	17%	3	0.4	0.0	16.2
	634.93976	33%	71%	4	0.8	0.1	12.1
	1406.7278	33%	83%				
	1714.1026	33%	92%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	126.95313	80%	12%	1			
	126.95313	80%	12%	2	1.3	0.0	152.2
	125	100%	12%	3	1.0	0.0	110.4
	634.93976	20%	71%	4	3.3	0.1	179.3
	1065.3846	20%	82%				
	1714.1026	20%	94%				
24 hours	126.95313	80%	12%	1			
	126.95313	80%	12%	2	1.3	0.0	152.2
	125	100%	12%	3	1.0	0.0	110.4
	634.93976	20%	71%	4	3.3	0.1	179.3
	1065.3846	20%	82%				
	1714.1026	20%	94%				
48 hours	126.95313	80%	12%	1			
	126.95313	80%	12%	2	1.3	0.0	152.2
	125	100%	12%	3	1.0	0.0	110.4
	634.93976	20%	71%	4	3.3	0.1	179.3
	1065.3846	20%	82%				
	1714.1026	20%	94%				

FIG. 7 - 4

Lactotransferrin

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	237.743	111.248	237.743	111.248	237.743	111.248
average	306.729	310.281	306.729	310.281	306.729	310.281
stdev	249.940	403.603	249.940	403.603	249.940	403.603
p (t-test)		0.985		0.985		0.985
min	68.170	69.910	68.170	69.910	68.170	69.910
max	828.017	1168.270	828.017	1168.270	828.017	1168.270
n (Samp)	7	7	7	7	7	7
n (Pat)	7	7	7	7	7	7

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	212.278	na	212.278	na	212.278	na
average	224.909	na	224.909	na	224.909	na
stdev	65.976	na	65.976	na	65.976	na
p (t-test)		na		na		na
min	162.964	na	162.964	na	162.964	na
max	312.118	na	312.118	na	312.118	na
n (Samp)	4	0	4	0	4	0
n (Pat)	4	0	4	0	4	0

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	186.813	102.763	186.813	102.763	186.813	102.763
average	319.449	334.834	319.449	334.834	319.449	334.834
stdev	303.819	436.361	303.819	436.361	303.819	436.361
p (t-test)		0.949		0.949		0.949
min	68.170	69.910	68.170	69.910	68.170	69.910
max	828.017	1168.270	828.017	1168.270	828.017	1168.270
n (Samp)	5	6	5	6	5	6
n (Pat)	5	6	5	6	5	6

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.39	0.155	7	7	0.469
24 hours	0.39	0.155	7	7	0.469
48 hours	0.39	0.155	7	7	0.469

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	nd	nd	4	0	nd
24 hours	nd	nd	4	0	nd
48 hours	nd	nd	4	0	nd

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.43	0.181	5	6	0.713
24 hours	0.43	0.181	5	6	0.713
48 hours	0.43	0.181	5	6	0.713

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	90.361473	71%	14%	1			
	69.910482	86%	14%	2	0.0	0.0	na
	68.169972	100%	14%	3	3.0	0.0	290.6
	312.11789	29%	71%	4	2.0	0.0	268.6
	362.19409	29%	86%				
	828.01688	14%	100%				

FIG. 7 - 5

24 hours	90.361473	71%	14%	1			
	69.910482	86%	14%	2	0.0	0.0	na
	68.169972	100%	14%	3	3.0	0.0	290.6
	312.11789	29%	71%	4	2.0	0.0	268.6
	362.19409	29%	86%				
	828.01688	14%	100%				
48 hours	90.361473	71%	14%	1			
	69.910482	86%	14%	2	0.0	0.0	na
	68.169972	100%	14%	3	3.0	0.0	290.6
	312.11789	29%	71%	4	2.0	0.0	268.6
	362.19409	29%	86%				
	828.01688	14%	100%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	69.910482	83%	20%	1			
	69.910482	83%	20%	2	0.0	0.0	na
	68.169972	100%	20%	3	na	na	na
	362.19409	33%	80%	4	0.5	0.0	476.7
	362.19409	33%	80%				
	828.01688	17%	100%				
24 hours	69.910482	83%	20%	1			
	69.910482	83%	20%	2	0.0	0.0	na
	68.169972	100%	20%	3	na	na	na
	362.19409	33%	80%	4	0.5	0.0	476.7
	362.19409	33%	80%				
	828.01688	17%	100%				
48 hours	69.910482	83%	20%	1			
	69.910482	83%	20%	2	0.0	0.0	na
	68.169972	100%	20%	3	na	na	na
	362.19409	33%	80%	4	0.5	0.0	476.7
	362.19409	33%	80%				
	828.01688	17%	100%				

FIG. 7 - 6

Prostatic Acid Phosphatase

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.173	0.250	0.173	0.250	0.173	0.250
average	0.268	0.895	0.268	0.895	0.268	0.895
stdev	0.421	2.083	0.421	2.083	0.421	2.083
p (t-test)		0.034		0.034		0.034
min	0.037	0.041	0.037	0.041	0.037	0.041
max	2.470	9.690	2.470	9.690	2.470	9.690
n (Samp)	56	21	56	21	56	21
n (Pat)	56	21	56	21	56	21

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.173	0.265	0.173	0.265	0.173	0.265
average	0.664	0.714	0.664	0.714	0.664	0.714
stdev	2.082	1.004	2.082	1.004	2.082	1.004
p (t-test)		0.959		0.959		0.959
min	0.041	0.234	0.041	0.234	0.041	0.234
max	9.690	2.510	9.690	2.510	9.690	2.510
n (Samp)	21	5	21	5	21	5
n (Pat)	21	5	21	5	21	5

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.177	0.319	0.177	0.319	0.177	0.319
average	0.276	0.387	0.276	0.387	0.276	0.387
stdev	0.438	0.246	0.438	0.246	0.438	0.246
p (t-test)		0.328		0.328		0.328
min	0.037	0.041	0.037	0.041	0.037	0.041
max	2.470	0.885	2.470	0.885	2.470	0.885
n (Samp)	46	17	46	17	46	17
n (Pat)	46	17	46	17	46	17

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.72	0.070	56	21	0.002
24 hours	0.72	0.070	56	21	0.002
48 hours	0.72	0.070	56	21	0.002

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.85	0.115	21	5	0.002
24 hours	0.85	0.115	21	5	0.002
48 hours	0.85	0.115	21	5	0.002

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.75	0.075	46	17	0.001
24 hours	0.75	0.075	46	17	0.001
48 hours	0.75	0.075	46	17	0.001

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.215	71%	71%	1			
	0.151	81%	46%	2	2.3	0.4	12.6
	0.141	90%	41%	3	3.0	0.6	15.5
	0.215	71%	71%	4	8.5	1.9	37.6
	0.269	48%	80%				
	0.439	33%	91%				

FIG. 7 - 7

24 hours	0.215	71%	71%	1			
	0.151	81%	46%	2	2.3	0.4	12.6
	0.141	90%	41%	3	3.0	0.6	15.5
	0.215	71%	71%	4	8.5	1.9	37.6
	0.269	48%	80%				
	0.439	33%	91%				
48 hours	0.215	71%	71%	1			
	0.151	81%	46%	2	2.3	0.4	12.6
	0.141	90%	41%	3	3.0	0.6	15.5
	0.215	71%	71%	4	8.5	1.9	37.6
	0.269	48%	80%				
	0.439	33%	91%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.226	71%	72%	1			
	0.215	82%	67%	2	2.0	0.1	50.1
	0.148	94%	41%	3	8.4	0.6	115.7
	0.226	71%	72%	4	14.0	1.1	186.6
	0.283	53%	80%				
	0.39	29%	91%				
24 hours	0.226	71%	72%	1			
	0.215	82%	67%	2	2.0	0.1	50.1
	0.148	94%	41%	3	8.4	0.6	115.7
	0.226	71%	72%	4	14.0	1.1	186.6
	0.283	53%	80%				
	0.39	29%	91%				
48 hours	0.226	71%	72%	1			
	0.215	82%	67%	2	2.0	0.1	50.1
	0.148	94%	41%	3	8.4	0.6	115.7
	0.226	71%	72%	4	14.0	1.1	186.6
	0.283	53%	80%				
	0.39	29%	91%				

FIG. 7 - 8

Erythropoietin receptor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	290.373	117.424	290.373	117.424	290.373	na
average	1032.036	206.018	1032.036	206.018	1032.036	na
stdev	1811.528	206.459	1811.528	206.459	1811.528	na
p (t-test)		0.437		0.437		na
min	12.346	58.642	12.346	58.642	12.346	na
max	8263.287	441.989	8263.287	441.989	8263.287	na
n (Samp)	55	3	55	3	55	0
n (Pat)	55	3	55	3	55	0

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	236.328	9.259	236.328	9.259	236.328	9.259
average	792.420	58.642	792.420	58.642	792.420	58.642
stdev	1489.255	na	1489.255	na	1489.255	na
p (t-test)		na		na		na
min	9.259	58.642	9.259	58.642	9.259	58.642
max	8263.287	58.642	8263.287	58.642	8263.287	58.642
n (Samp)	92	1	92	1	92	1
n (Pat)	92	1	92	1	92	1

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	352.484	117.424	352.484	117.424	352.484	na
average	1075.016	206.018	1075.016	206.018	1075.016	na
stdev	1674.425	206.459	1674.425	206.459	1674.425	na
p (t-test)		0.378		0.378		na
min	12.346	58.642	12.346	58.642	12.346	na
max	6805.195	441.989	6805.195	441.989	6805.195	na
n (Samp)	47	3	47	3	47	0
n (Pat)	47	3	47	3	47	0

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.27	0.127	55	3	0.073
24 hours	0.27	0.127	55	3	0.073
48 hours	nd	nd	55	0	nd

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.05	0.056	92	1	0.000
24 hours	0.05	0.056	92	1	0.000
48 hours	0.05	0.056	92	1	0.000

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.27	0.127	47	3	0.070
24 hours	0.27	0.127	47	3	0.070
48 hours	nd	nd	47	0	nd

FIG. 8 - 1

Intercellular adhesion molecule 1

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	205637.010	319174.717	205637.010	319174.717	205637.010	319174.717
average	262966.542	382655.529	262966.542	382655.529	262966.542	436571.985
stdev	175123.670	210891.799	175123.670	210891.799	175123.670	328156.163
p (t-test)		0.061		0.061		0.107
min	51907.253	193433.392	51907.253	193433.392	51907.253	183261.199
max	1060572.701	807280.039	1060572.701	807280.039	1060572.701	807280.039
n (Samp)	75	9	75	9	75	3
n (Pat)	75	9	75	9	75	3

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	206039.902	403943.289	206039.902	403943.289	206039.902	569880.435
average	257720.863	478070.920	257720.863	478070.920	257720.863	569880.435
stdev	156303.703	248377.088	156303.703	248377.088	156303.703	335733.739
p (t-test)		0.003		0.003		0.007
min	51907.253	193433.392	51907.253	193433.392	51907.253	332480.831
max	1060572.701	807280.039	1060572.701	807280.039	1060572.701	807280.039
n (Samp)	129	5	129	5	129	2
n (Pat)	129	5	129	5	129	2

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	216297.678	292610.964	216297.678	292610.964	216297.678	319174.717
average	281083.446	365551.005	281083.446	365551.005	281083.446	436571.985
stdev	159164.302	221172.194	159164.302	221172.194	159164.302	328156.163
p (t-test)		0.235		0.235		0.121
min	51907.253	204249.960	51907.253	204249.960	51907.253	183261.199
max	766357.408	807280.039	766357.408	807280.039	766357.408	807280.039
n (Samp)	61	6	61	6	61	3
n (Pat)	61	6	61	6	61	3

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.73	0.100	75	9	0.024
24 hours	0.73	0.100	75	9	0.024
48 hours	0.71	0.172	75	3	0.229

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.80	0.121	129	5	0.014
24 hours	0.80	0.121	129	5	0.014
48 hours	0.88	0.158	129	2	0.016

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.66	0.127	61	6	0.211
24 hours	0.66	0.127	61	6	0.211
48 hours	0.67	0.176	61	3	0.327

FIG. 8 - 2

Lactotransferrin

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	195.705	89.491	195.705	89.491	195.705	102.980
average	422.167	412.908	422.167	412.908	422.167	338.302
stdev	481.397	540.081	481.397	540.081	481.397	431.931
p (t-test)		0.967		0.967		0.776
min	26.292	61.643	26.292	61.643	26.292	75.132
max	1474.768	1324.895	1474.768	1324.895	1474.768	836.793
n (Samp)	25	6	25	6	25	3
n (Pat)	25	6	25	6	25	3

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	160.337	836.793	160.337	836.793	160.337	455.963
average	393.162	745.607	393.162	745.607	393.162	455.963
stdev	452.252	629.851	452.252	629.851	452.252	538.576
p (t-test)		0.207		0.207		0.849
min	26.292	75.132	26.292	75.132	26.292	75.132
max	1474.768	1324.895	1474.768	1324.895	1474.768	836.793
n (Samp)	44	3	44	3	44	2
n (Pat)	44	3	44	3	44	2

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	237.743	89.491	237.743	89.491	237.743	469.887
average	433.325	269.355	433.325	269.355	433.325	469.887
stdev	476.202	378.680	476.202	378.680	476.202	518.884
p (t-test)		0.519		0.519		0.918
min	26.292	61.643	26.292	61.643	26.292	102.980
max	1474.768	836.793	1474.768	836.793	1474.768	836.793
n (Samp)	25	4	25	4	25	2
n (Pat)	25	4	25	4	25	2

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.44	0.129	25	6	0.642
24 hours	0.44	0.129	25	6	0.642
48 hours	0.47	0.176	25	3	0.850

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.64	0.179	44	3	0.420
24 hours	0.64	0.179	44	3	0.420
48 hours	0.50	0.211	44	2	1.000

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.37	0.142	25	4	0.360
24 hours	0.37	0.142	25	4	0.360
48 hours	0.58	0.222	25	2	0.718

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	71.650992	83%	20%	1			
	71.650992	83%	20%	2	0.0	0.0	na
	42.482162	100%	12%	3	1.0	0.1	13.6
	360.84388	33%	72%	4	1.2	0.1	17.5
	742.27848	33%	80%				
	1266.1603	17%	92%				

FIG. 8 - 3

24 hours	71.650992	83%	20%	1			
	71.650992	83%	20%	2	0.0	0.0	na
	42.482162	100%	12%	3	1.0	0.1	13.6
	360.84388	33%	72%	4	1.2	0.1	17.5
	742.27848	33%	80%				
	1266.1603	17%	92%				
48 hours	71.650992	100%	20%	1			
	71.650992	100%	20%	2	0.0	0.0	na
	71.650992	100%	20%	3	1.0	0.0	96.9
	360.84388	33%	72%	4	1.0	0.0	96.9
	742.27848	33%	80%				
	1266.1603	0%	92%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	71.650992	100%	18%	1			
	71.650992	100%	18%	2	0.0	0.0	na
	71.650992	100%	18%	3	0.0	0.0	na
	360.84388	67%	70%	4	2.0	0.1	56.0
	828.01688	67%	82%				
	1214.8523	33%	91%				
24 hours	71.650992	100%	18%	1			
	71.650992	100%	18%	2	0.0	0.0	na
	71.650992	100%	18%	3	0.0	0.0	na
	360.84388	67%	70%	4	2.0	0.1	56.0
	828.01688	67%	82%				
	1214.8523	33%	91%				
48 hours	71.650992	100%	18%	1			
	71.650992	100%	18%	2	0.0	0.0	na
	71.650992	100%	18%	3	0.0	0.0	na
	360.84388	50%	70%	4	1.1	0.0	80.6
	828.01688	50%	82%				
	1214.8523	0%	91%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	71.650992	75%	20%	1			
	42.482162	100%	12%	2	0.0	0.0	na
	42.482162	100%	12%	3	1.2	0.0	107.9
	364.21941	25%	72%	4	2.8	0.1	103.7
	742.27848	25%	80%				
	1266.1603	0%	92%				
24 hours	71.650992	75%	20%	1			
	42.482162	100%	12%	2	0.0	0.0	na
	42.482162	100%	12%	3	1.2	0.0	107.9
	364.21941	25%	72%	4	2.8	0.1	103.7
	742.27848	25%	80%				
	1266.1603	0%	92%				
48 hours	99.064023	100%	36%	1			
	99.064023	100%	36%	2	na	na	na
	99.064023	100%	36%	3	na	na	na
	364.21941	50%	72%	4	na	na	na
	742.27848	50%	80%				
	1266.1603	0%	92%				

FIG. 8 - 4

Prostatic Acid Phosphatase

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.181	0.458	0.181	0.347	0.181	0.321
average	0.728	0.552	0.728	0.507	0.728	0.375
stdev	4.459	0.563	4.459	0.582	4.459	0.268
p (t-test)		0.872		0.839		0.803
min	0.025	0.084	0.025	0.076	0.025	0.030
max	47.000	2.510	47.000	2.510	47.000	1.020
n (Samp)	111	17	111	17	111	10
n (Pat)	111	17	111	17	111	10

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.215	0.471	0.215	0.471	0.215	0.351
average	0.665	0.661	0.665	0.661	0.665	0.347
stdev	3.580	0.760	3.580	0.760	3.580	0.179
p (t-test)		0.997		0.997		0.843
min	0.025	0.097	0.025	0.097	0.025	0.076
max	47.000	2.510	47.000	2.510	47.000	0.531
n (Samp)	179	8	179	8	179	5
n (Pat)	179	8	179	8	179	5

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	0.181	0.347	0.181	0.278	0.181	0.278
average	0.847	0.438	0.847	0.368	0.847	0.340
stdev	4.977	0.295	4.977	0.319	4.977	0.316
p (t-test)		0.787		0.752		0.789
min	0.000	0.084	0.000	0.076	0.000	0.030
max	47.000	1.020	47.000	1.020	47.000	1.020
n (Samp)	89	11	89	11	89	7
n (Pat)	89	11	89	11	89	7

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.75	0.072	111	17	0.001
24 hours	0.68	0.076	111	17	0.020
48 hours	0.70	0.096	111	10	0.042

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.75	0.101	179	8	0.012
24 hours	0.75	0.101	179	8	0.012
48 hours	0.65	0.135	179	5	0.273

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.73	0.090	89	11	0.010
24 hours	0.62	0.095	89	11	0.196
48 hours	0.63	0.117	89	7	0.285

sCr or UO

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.294	71%	75%	1			
	0.205	82%	57%	2	0.0	0.0	na
	0.0964	94%	17%	3	2.8	0.6	12.6
	0.266	76%	70%	4	6.8	1.8	25.8
	0.344	65%	80%				
	0.584	18%	90%				

FIG. 8 - 5

24 hours	0.205	71%	57%	1			
	0.163	82%	45%	2	0.3	0.0	4.8
	0.0784	94%	12%	3	1.4	0.4	5.0
	0.266	65%	70%	4	3.8	1.4	10.5
	0.344	53%	80%				
	0.584	18%	90%				
48 hours	0.272	70%	73%	1			
	0.205	80%	57%	2	0.0	0.0	na
	0.204	90%	57%	3	4.5	0.3	59.6
	0.266	70%	70%	4	5.6	0.5	67.6
	0.344	50%	80%				
	0.584	10%	90%				

sCr only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.422	75%	82%	1			
	0.293	88%	68%	2	0.0	0.0	na
	0.0964	100%	16%	3	1.0	0.0	53.7
	0.314	75%	70%	4	6.6	0.6	71.0
	0.4	75%	80%				
	0.758	13%	91%				
24 hours	0.422	75%	82%	1			
	0.293	88%	68%	2	0.0	0.0	na
	0.0964	100%	16%	3	1.0	0.0	53.7
	0.314	75%	70%	4	6.6	0.6	71.0
	0.4	75%	80%				
	0.758	13%	91%				
48 hours	0.293	80%	68%	1			
	0.293	80%	68%	2	0.0	0.0	na
	0.075	100%	9%	3	2.0	0.1	42.3
	0.314	60%	70%	4	2.0	0.1	42.3
	0.4	40%	80%				
	0.758	0%	91%				

UO only

Time prior AKI stage	Cutoff value	sens	spec	Quartile	OR	95% CI of OR	
0 hours	0.293	73%	74%	1			
	0.205	82%	56%	2	0.0	0.0	na
	0.199	91%	56%	3	4.6	0.3	63.1
	0.268	73%	71%	4	7.6	0.6	89.7
	0.344	55%	81%				
	0.672	18%	91%				
24 hours	0.199	73%	56%	1			
	0.163	82%	44%	2	0.5	0.0	10.7
	0.0784	91%	15%	3	2.2	0.4	11.4
	0.268	55%	71%	4	2.2	0.4	11.4
	0.344	36%	81%				
	0.672	18%	91%				
48 hours	0.205	71%	56%	1			
	0.199	86%	56%	2	0.0	0.0	na
	0.000342	100%	1%	3	4.6	0.3	64.0
	0.268	57%	71%	4	2.1	0.1	47.1
	0.344	29%	81%				
	0.672	14%	91%				

FIG. 8 - 6

von Willebrand Factor

sCr or UO

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	104.000	143.000	104.000	143.000	104.000	136.000
average	111.046	163.035	111.046	161.765	111.046	150.470
stdev	39.391	60.467	39.391	60.189	39.391	48.453
p (t-test)		0.000		0.000		0.004
min	32.000	94.600	32.000	94.400	32.000	92.700
max	278.000	328.000	278.000	328.000	278.000	224.000
n (Samp)	111	17	111	17	111	10
n (Pat)	111	17	111	17	111	10

sCr only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	107.000	143.000	107.000	143.000	107.000	143.000
average	113.492	145.750	113.492	145.050	113.492	145.000
stdev	42.272	33.763	42.272	34.886	42.272	29.504
p (t-test)		0.035		0.039		0.100
min	32.000	100.000	32.000	94.400	32.000	117.000
max	328.000	210.000	328.000	210.000	328.000	194.000
n (Samp)	179	8	179	8	179	5
n (Pat)	179	8	179	8	179	5

UO only

	0 hr prior to AKI stage		24 hr prior to AKI stage		48 hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
median	104.000	143.000	104.000	143.000	104.000	129.000
average	109.143	175.691	109.143	174.236	109.143	155.814
stdev	36.579	71.199	36.579	70.589	36.579	58.185
p (t-test)		0.000		0.000		0.003
min	32.000	94.600	32.000	94.600	32.000	92.700
max	240.000	328.000	240.000	328.000	240.000	224.000
n (Samp)	89	11	89	11	89	7
n (Pat)	89	11	89	11	89	7

sCr or UO

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.79	0.068	111	17	0.000
24 hours	0.79	0.068	111	17	0.000
48 hours	0.75	0.092	111	10	0.006

sCr only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.76	0.100	179	8	0.008
24 hours	0.75	0.101	179	8	0.012
48 hours	0.78	0.123	179	5	0.022

UO only

Time prior AKI stage	AUC	SE	nCohort 1	nCohort 2	p
0 hours	0.81	0.081	89	11	0.000
24 hours	0.81	0.081	89	11	0.000
48 hours	0.74	0.111	89	7	0.029

FIG. 8 - 7