KIDNEY

* How to classify an acute kidney injury?
* Chronic kidney disease.
* Treatment.

Renal failure is a general form and is a little bit old

**Acute kidney injury:**

The term acute renal failure was used to describe abrupt rapid declined renal function 8-10 years ago.

Due to the variability in the definitions upon research studies we needed to come up with one definition for the acute kidney injury.

Some of the definitions depended on certain varieties; change in creatinin, absolute rise in creatinine, is it the change in the urine nitrogen?, is it the change in the urine output?, is it the need for renal replacement therapy….etc.

* **Classification of the acute kidney injury:**

**RIFLE** Criteria: (in 2002)

R: for RISK

I: for INJURY

F: for FAILURE

L: for LOSS

E: for END STAGE RENAL DISEASE; there is no reversal for the cause and the patient will stay on renal replacement therapy (dialysis or transplant).

1-Risk: they apply there code change in creatinine. For example, if the patient has creatinine of 1 fold, you need this to be at least 1.5 fold or you need his GFR to decrease by 25% to put him in the risk group, or you need his urine output to decrease by 0.5 mL/kg/hour for at least 6 hours.

Every stage in these stages has a definition according to the rise in the creatinine and according to the change in the urine output.

|  |  |  |
| --- | --- | --- |
| **Category** | **GFR Criteria** | **Urine Output Criteria** |
| Risk | Increased creatinine ×1.5GFR decrease >25% | UO < 0.5 mL/kg/h × 6 hr |
| Injury | Increased creatinine ×2GFR decrease >50% | UO < 0.5 mL/kg/h × 12 hr |
| Failure | Increase creatinine ×3GFR decrease >75% | UO < 0.3 mL/kg/h × 24 hrAnuria × 12 hr |
| Loss | Persistent ARF = complete loss of kidney function >4 weeks |  |
| ESKD | End-stage kidney disease (>3 months) |  |

ARF, acute renal failure; GFR, glomerular filtration rate; RIFLE, ***r***isk of renal dysfunction

Notice that we didn't use the renal replacement therapy. That's why 2 years later most institutions that work in nephrology worldwide came out with a new classification called **AKIN**:

A: for ACUTE

K: for KIDNEY

I: for INJURY

N: for NETWORK

AKIN CRITERIA:

It was divided into 3 stages:

|  |  |  |
| --- | --- | --- |
| Stage | Creatinine | Urine Output |
| 1 | Increase 1.5-2 folds from the baseline | Less than 0.5mL/kg/hour for more than 6 hours |
| 2 | Increase 2-3 folds from the baseline | Less than 0.5mL/kg/hour for at least 12 hours |
| 3 | Increase 3 folds from the baseline or any renal replacement therapy  | Less than 0.3mL/kg/hourfor 24 hours or anuria for 12 hours  |

Why did they come up with the RIFLE and AKIN criteria?

In the sake of research. Any research done were they want to define the acute injury, they must say which classification of kidney injury they used.

* ***Acute kidney injury:*** is the increase in the serum creatinine over hours to days.

Hours; it's subacute if we have increase in days to weeks, and becomes **Chronic**; if the increase lasts from weeks to months

* It can be oligouric or nonoligouric

Oligouric: how much is the patients urine output/day

Daily urine volume of less than 400 mL.

Non-oligouric: if the urine output/day >400mL or 500mL

Example:

2 patients with acute kiney injurey, one of them has urine output and the other doesn't. Both of them have kidney injury but one of them is oligouric and the other is non-oligouric, this depends on the clearance.

* **Causes of acute kidney injury:**
1. Is it pre-renal (a problem before reaching the kidneys)?
2. Is it renal (something intrinsic involving the kidneys)?
3. Is it post-renal (in the urinary system, related to the bladder outlet, the ureters or the urethra….)

The easiest thing is to rule out the third cause (post-renal) because its causes are limited.

For example, If it was an old patient with post-renal acute kidney injury the obstructions would mostly be benign prosthetic hyperplasia (most common cause), but if the patient was at a younger age ,20 or 30 years old, we would have to think of other causes such as kidney stones.

* **Pre-renal acute kidney failure:**

It is related to the low GFR because of low renal blood flow, and if you correct the renal blood flow you will find that the GFR will increase very quickly, and you won't have any structural bases or structural changes related to this type of acute kidney injury.

For example; a patient with diarrhea, vomiting or any cause of blood loss he will have hemodynamic instability (hypotension, intravascular volume decreases), the kidneys will feel this decrease, and an automatic decrease in the GFR occurs (pre-renal response to a sudden reduction in [blood flow to the kidney](http://www.webmd.com/kidney-stones/blood-supply-to-the-kidneys)).

* **Normal response to low blood pressure (GFR auto regulation):**

When low blood pressure occurs in this case (systemic low blood pressure or low intravascular volume), the kidney tries to treat the situation through the intrinsic mechanism GFR autoregulation;

1. the kidney tries to do afferent arteriolar dilatation to collect as much as it can blood to the kidneys.
2. local increase of renal prostaglandin synthesis which causes vasodilatation which helps to drag more blood to the kidneys.
3. At the same time we need to maintain intraglomerular pressure because we want to maintain the GFR as much as possible. So, the afferent blood vessels open on one side, and vasoconstriction to the efferent to maintain the intraglumeral pressure as much as possible.

A normal patient with blood pressure 120/80, his GFR is 120mL/minute. Usually the afferent have a more thicker muscular layer.

Hypotension occurred 90/60, the GFR is still the same, what happens is maximum vasodilation to the afferent (relaxation to the smooth muscles) at the same time vasoconstriction at the efferent through the angiotensin-2.

This is activation of the RAS system; it comes out when there is activation of the hypertension or arrangement of the intravascular volumes.

If fluids are supplied and tension is increased the intravascular volume is modified, shutdown to the RAS system and everything returns back to normal.

No structural changes or any damage at the level of the kidney.

* **What factors would derange autoregulation the level of the GFR?**
1. In the chronic kidney disease we will have maximum afferent dilatation, so the kidney won't be able to do any extra widening in the case of acute kidney injury and this will cause more incidence of having an acute kidney injury in the patient of advanced chronic kidney disease.
2. Non-steroidal and COX-2 inhibit the prostaglandin, no local vasodilatation exists anymore. This will derange the autoregulation.
3. Base inhibitors and ARBs (angiotensin -2 receptor blockers) will block the activation of the RAS system, no angiotensin-2, so no vasoconstriction of the efferent, so shutdown and loss of intraglumeral pressure.
4. Chronic vascular disease; If the patient has atherosclerosis because of age, hypertension and so on, the flexibility or the elasticity of the vessels is not that much, so the response for the RAS system or the autoregulatory mechanism won't be as is it's supposed to.

 If these causes exist they will increase the likelihood of getting structural injury related to acute kidney injury.

Prerenal failure is either related to the low blood pressure from any cause or to the failure of the pump.

A patient with extracellular fluid volume depletion (diarrhea, vomiting, hemorrhage, bleeding), cardiogenic (the pump itself isn't working; heart failure), blood won't reach the kidneys (as if we have intravascular volume depletion; but here there isn't any pump for blood to reach the kidneys).

 Any cause will cause systemic vasodilation; stasis in the intravascular volume, so it doesn't supply the kidneys with enough blood. Such as the cases of sepsis and liver disease are of generalized vasodilatation with low blood pressure, acute kidney injury could occur in these cases.

* ***Local renal vasoconstriction***; not systematic vasoconstriction

Patients taking cyclosporine or tacrolimus are usually Glomerular nephritis (GN) or transplant patients (renal, liver, lungs), vasculitis patients (connective tissue disease). These drugs are immunosuppressive and at the same time have the feature to do renal vasoconstriction.

Catecholamines, amphetamines (redbull), cocaine, antibiotics (amphotericin "antifungal"), and patients with hypercalcemia could be affected with local renal failure.

* **How to diagnose a critical injury?**

Usually you need to take history and physical examination to any disease and investigation is done at the end to diagnose it.

Very obvious history (fluid imbalance, taking drugs, etc. that gives me a hint that there is intravascular volume depletion).

 Physical examination is about blood pressure (patients with low blood pressure are expected to have intravascular volume depletion. If it wasn't low we have to elicit postural changes; you let the patient stand up and then measure his blood pressure once again. If there are significant postural changes were the blood pressure decreases upon standing then this means he has obscure intravascular volume depletion but it didn't appear only in his standing position).

That's why vital signs are taken in both the sitting and standing situation looking for postural changes that usually exist when there is more than 10% loss of the intravascular volume.

 Clinical wise bedside you have to take care of the jugular vein pressure, the GVV (glomerular volume variation), if the patient was in the ICU the CVP (central venous pressure), other signs of volume over…. In the cases of heart failure or liver disease they would have interstitial renal sequestration but they wouldn't have intravascular volume depletion (good volume).

* **Urine analysis**; Should be blood, there are no structural changes so we won't find any damage at the level of the kidney.
* **Urine electrolytes**; sodium is the most important (the sodium is going hand in hand with water; losing sodium means losing water and vise versa). If urine sodium less than 20mL/L means that the kidneys are trying their best to preserve as much as possible (there isn't less than 20mL/L), if it were 10mL/L this means that the kidneys are doing extra effort to preserve water ( because we can't measure the water so we measure the sodium inside the urine), if the sodium was more than 20mL/L this means I'm losing sodium, water which means that there is some sort of structure changes and there is no pre-renal failure as a diagnosis.
* **Renal causes of acute kidney injury** :

 By anatomy, when we think of the intrinsic causes for acute kidney injury we have to remember that the kidney is composed of the vascular compartment, cortex were glomerular part exists, the tubular and the in between interstitium. Any derangement in any of these 4 divisions can give us kidney injury.

Thrombotic microangiopathy (TMA), Acute renal artery occlusion can occur in the vascular part and could lead to acute renal injury.

In the glomerular part, glomerular nephritis might occur.

In the tubular part, acute tubular necrosis (ATM) might occur.

 In the interstitium part, acute interstitial nephritis might occur.

**The most common cause for acute kidney injury (intrinsic renal causes by frequency) is by far ischemic ETM;** restructural changes, extreme prerenal acute kidney injury, were the kidneys preserve the flow as much as possible, but at the end the autoregulatory mechanism will fail, structural changes will occur, urine analysis changes.

Most of the time in the ischemic ETM heme granular cast is found in the urine analysis.

**Chronic kidney disease:**

This is a very common case.

Example:

A 65 year old lady referred with diabetic nephropathy, she has protein urea with 3g/day (the patient is entering nephritic syndrome, in a normal case protein urea is supposed to be <300mg/24hr), her GFR is 23, she didn't have nausea, vomiting, weight loss or anorexia and only noted some sort of meat aversion (she feels sick when eating meat). Her medications include amlodipine and hydrochlorothiazide, her blood presseure is 150/90mmHg (high), her hemoglobin is 8.9 (low-anemia), potassium 5.6 (high- hyperkalemia), calcium is 7 (low- hypocalcemia), phosphorus is 6 (high), PTH is 300 (high) and the LDL is high (it should be <70).

* **The main cause of anemia:**

 The kidney is the main source of erythropoietin, so when an advanced stage of chronic kidney disease is reached more loss of erythropoietin occurs, and these patients tend to have anemia.

Also, these patients when reaching the advanced stage of chronic kidney disease (low stage of GFR increases the urea) stop eating mostly good sources of protein because there will be urea because proteins turns into urea in the body (nutritional deficiencies, iron deficiency, erythropoietin deficiency, etc.).

* **The main cause of increase in phosphorus and decrease in calcium:**

The kidney has part in activation of vitamin D (site 1), if there is kidney failure there won't be fully active vitamin D so the patient will start having hypocalcemia as a first step were it's very important to absorb the calcium from the guts and to reabsorb it from the kidney.

How to counteract hypocalcemia? The parathyroid will be activated and the PTH will increase.

No good urine output, so the phosphorus will accumulate because we have low urine output due to the low GFR. The PTH won't be able to work on the kidneys as it's supposed to because of the low GFR.

So the main cause isn't related to the PTH because the PTH is supposed to increase the secretion of the phosphorus inside the urine.

* **Hyperkalemia:**

To get rid of potassium I need a good urine flow, a good GFR, the GFR starts to decrease so these patients tend to gain potassium.

Most food we eat contains potassium. The source is already there, but decrease in excretion will cause hyperkalemia.

* ***Kidney disease outcomes quality initiative (K/DOQI)***; it's mission is to come out with definitions and general guidelines to be adapted all over the world.

Any nephrologist should adapt these guidelines and try as much as possible to work with them.

***Chronic kidney disease (CKD):*** is kidney damage for at least 3 months as defined by structural or functional abnormality with or without GFR decrease.

If a patient with creatinine 0.5mg/dL (normal baseline). He had acute kidney injury were the creatinine rised up to 1.5mg/dL. In this case we have to give this patient time for his acut kidney injurey to be reversed. If he/she didn't regain their baseline within 3 months this means it's a new baseline which is related to damage and the patient is entering chronic kidney disease stage.

A patient with a kidney disease and urine secretion would have good GFR, and his urine secretion depends on whether it's a structural or functional abnormality.

* **Functional abnormalities**: positive haematuria (presence of blood in urine), some sort of abnormality that will lead them later on to progression to other stage of chronic kidney disease.
* **Structural changes:** we need to be aware that they have chronic kidney disease then we need to intervene.

Patients with polycystic kidney disease are normal 100%, normal GFR until years pass some abnormalities start to appear. But we're not supposed to wait all these years until we get to notice them having chronic disease, we should treat them from the beginning.

Patients of renal transplant, even if there GFR and creatinine were normal they are at risk later on of progression to other stages of CKD. That's why we consider them CKD patients.

A patient with GFR<60 to begin with for more than 3 months.

* **Stages of CKD:**

Stage1: Normal GFR, with abnormal function or abnormal structure (patients with risk factors for progression later on to CKD).

Stage 2: GFR (60-89 mL/hour) with persistent of structural or functional abnormality.

Stage3: GFR (30-59 mL/hour).

Stage4: GFR (15-29 mL/hour)

Stage 5: End stage renal disease, when the GFR <15mL/hour

Most symptoms related to the CKD (loss of function related to anemia, decrease in vitamin D, erythropoietin, acidosis and so on) usually start when the GFR < 60 mL/hour (after stage 3).

We have normal progression of chronic kidney disease. GFR tends to decline simply over time. But, when the loss of GFR is very quick we must interpret in order to delay the progression to the end stage renal disease.

What happens in the CKD is an initial injury (stage of acute kidney injury), if acute tubular necrosis, acute interstitial nephritis, they will lose the renal parenchyma. So, adaptive hyperfiltration starts to compensate, were the single nephron GFR increases.

Imagine that 1/3 the kidney was injured, what is the function of the rest of the glomeruli?

To take over. The GFR shouldn't decrease.

*Note: the kidney differs from the lung. In the respiratory disease not all the alveoli are used, so maximization occurs and all the alveoli are used. But in the kidneys all the glomeruli are working and what happens when loss occurs is that they must take over more work (hyperfiltration; increase in the intraglomerular pressure at the level of single nephron).*

*This causes more wallstress on the vessls which is a stimulus for increased secretion of TGF-beta (transformic growth factor) which is usually attractive for fibroblasts. The fibroblasts will cause fibrosis and long term damage to the remaining nephron and other complications occur (proteinuria, progression to more renal insufficiency).*

* **Changes in renal hemodynamics:** (the same as autoregulation)

In the chronic kidney disease there is maximum afferon hyperdilatation they cannot do more or do further about their injury.

* **Ways to assist the GFR:**
1. Equations to get the estimated GFR; MDRD equation and the Cockcroft-Gault.
2. Assessment of creatinine clearance through 24 hour urine collection
3. To use the radionuclide market (more accurate) in order to know the split functions of the kidneys.

(A patient saying one of his kidneys works for 40% and the other 55% knew this through the split function were he/she was given a radionulei material and every kidney was seen how much material it secretes, then split function of the kidney was measured indirectly).

This is very important when you need very accurate assessment for the kidneys. For example, in the case of renal transplant I need to do a very accurate assessment because not any kidney is taken haphazardly, we leave the patient with the better kidney and take the weaker one to transplant it in the patient.

* **Investigations of CKD:**

You need to differentiate between acute kidney injury and CKD.

A patient with GFR<60mL/hour, we don't know if it's acute where I can reverse it or chronic that cannot be reversed.

So our aim is to find a cause or a hint to say this is a chronic or an acute.

1. Urine analysis: if significant abnormalities exist this goes with chronic more than acute.
2. Kidneys size; a patient with high creatinine, upon ultrasound you found them with bilateral small kidneys….this is chronic.

But having normal sized kidneys doesn't rule out having CKD, other investigations (causes) are needed.

1. If he has pre-serum creatinine values, with his creatinine today 1.5mL/kg while it was 0.5 mL/kg a week ago,this is an acute case.

So, the baseline creatinine will help in deciding the case being acute or chronic.

1. Hemoglobin; patients with anemia (chronic)
2. Patients with mineral metabolism abnormalities such as calcium, potassium and phosphorus (chronic).
* **When do I go for biopsy?**

Sometimes it's used to differentiate, especially when neither history nor physical examination give me any hint. Because the proper diagnosis will help to differ in the long term management and long term intervention.

* **Factors implicated in the progression of CKD:**
1. Uncontrolled blood pressure (systemic hypertension)
2. Untreated proteinuria
3. Hyperlipidemia
4. Unlimited diet-protein intake
5. Angiotensin-2 or ergosterol on board
6. Metabolic acidosis
7. Hyperphosphatemia
8. Hyperuricemia

All these could be implicated in rapid loss of kidney function.

* **General management of CKD:**

Is treat the reversible causes.

1. Prevention way to slow progression
2. If any complications exist we treat them.
3. To decide when this patient will go to renal replacement therapy.

For example: if the patient is taking a lot of proteins, solution is protein restriction.

Aim of blood pressure is < 130/80.

Giving ….. in case of acidosis

Treatment of hyperlipidemia

* **Complications of CKD:**
1. Abnormalities in potassium (hyperkalemia)
2. Volume overload because of the low GFR
3. Metabolic acidosis
4. Anemia
* **Dialysis:** 2 types:
1. Hemodialysis; using the blood
2. Peritoneal dialysis; using the peritoneum were the patient fills his abdomen with a cleansing liquid called dialysis solution.  The walls of your abdominal cavity are lined with a membrane called the peritoneum, which allows waste products and extra fluid to pass from your blood into the dialysis solution. These wastes and fluid then leave your body when the dialysis solution is drained.

**Ultimate treatment of CKD:** transplant

***Are we dialyzing according to the GFR?*** "is every patient reaching the end stage renal disease treated with dialysis"

No, indications for dialysis must be looked for. If they don't exist it must be postponed because they noticed if we start treating these patients early just for the seek of the GFR there survival would be less than others.