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UREMIC CARDIOMYOPATHY

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SUMMARY

Introduction. Chronic kidney disease (CKD) is common, affecting one in seven of Western populations. There is a well-documented graded inverse relationship between cardiovascular risk and estimated glomerular filtration rate (eGFR) that is independent of age, sex and other risk factors.
Goal. To review the literature of patients with uremic cardiopathy.
Materials and methods. Review of modern and foreign literary sources; methods – description, analysis, abstracting.
Results and their discussion. The work is described in detail chronic kidney disease, uremic cardiomyopathy, causes, pathogenesis, complications.
Conclusions. Uremic cardiopathy depends largely on non-specific and potentially reversible factors such as anemia, hypertension and over hydration. It is the association and long-term persistence of these factors that are relatively specific to uremia.

Key words: arrhythmia, transplantation, hypertension, left ventricular hypertrophy, dialysis, chronic renal failure, QT interval.

Introduction. Chronic kidney disease (CKD) is common, affecting one in seven of Western populations.

There is a well-documented graded inverse relationship between cardiovascular risk and estimated glomerular filtration rate (eGFR) that is independent of age, sex and other risk factors.

Patients with CKD have an increased risk of coronary artery disease and an even higher risk of death from heart failure, arrhythmias and sudden death, which rises steeply with more severe CKD.

Pathological structural and functional remodeling occurs in the heart and vascular system in CKD. Left ventricular hypertrophy (LVH) is found in over 70% of patients with ESRD and other manifestations of heart muscle disease such as focal scarring and diffuse interstitial fibrosis (DIF) frequently occur, comprising the phenotype of uremic cardiomyopathy. These findings are also present to a lesser degree in early stage disease.

Hypertension is near universal. Vascular calcification is common and results from accelerated atherosclerosis (intimal disease) and arteriosclerosis (medial disease).

Regardless of the vascular bed affected, these changes confer elevated cardiac risk by increasing arterial stiffness, which can be measured by pulse wave velocity and augmentation index. These arterial changes increase LV after load which, together with humoral hypertrophic and profibrotic stimuli, leads to the syndrome of uremic cardiomyopathy.

Uremic Cardiomyopathy

Uremic cardiomyopathy serves as the arrhythmogenic substrate and triggers related to dialysis or cardiomyocyte metabolism may lead to a fatal arrhythmia. When evaluating in CKD patients the existence of a cardiomyopathy that serves as an arrhythmogenic substrate, the high prevalence of LVH draws attention first.

Uremic cardiomyopathy is a classic complication of chronic renal failure whose cause is unclear and treatment remains disappointing. Insulin resistance is an independent predictor of cardiovascular mortality in chronic renal failure. Underlying insulin resistance are defects in insulin signaling through the protein kinase, Akt. Akt acts as a nodal point in the control of both the metabolic and pleiotropic effects of insulin. Imbalance among these effects leads to cardiac hypertrophy, fibrosis, and apoptosis; less angiogenesis; metabolic remodeling; and altered calcium cycling, all key features of uremic cardiomyopathy.

Here we consider the role of Akt in the development of uremic cardiomyopathy, drawing parallels from models of hypertrophic cardiac disease.

The complex pathogenesis of uremic cardiomyopathy is incompletely understood, with many classical and renal-specific factors contributing to its expression. In contrast to the general population, the relative importance of atherosclerotic coronary disease is diminished in CKD, and that of left ventricular hypertrophy (LVH), heart failure, and sudden cardiac death are increased, although many of these complications are well represented in this renal population.

Experimental studies identify several intracellular signaling pathways vital to the pathogenesis of LVH, a key feature of uremic cardiomyopathy. Of these, the phosphoinositide-3 kinase (PI3K)-Akt pathway is of particular interest, for its role not only in regulating the development of LVH but also in postnatal coronary angiogenesis, cardiac fibrosis, cellular apoptosis, and metabolic dysfunction.

Furthermore, insulin resistance produces maladaptive alterations in the Akt pathway, enhancing its contribution to the development of uremic cardiomyopathy.

The cardinal features of uremic cardiac disease are LVH, reduced capillary density, fibrosis, and ventricular remodeling. Of these, LVH is predominant, increasing in prevalence from 26% of patients with stage 3 CKD to 75% of hemodialysis patients.

Hypertrophy is a powerful independent predictor of survival in CKD 54, 55 and regression of LVH is associated with reduced cardiovascular risk and improved survival.

Ventricular Hypertrophy

Cardiac hypertrophy is an adaptive response to a variety of physiologic and pathologic stresses; however, hypertrophied hearts are more susceptible to injury and ventricular dysfunction, and epidemiologic studies show that LVH triggers a cascade of detrimental changes ultimately resulting in heart failure.

In the postnatal period, normal cardiac growth and physiologic hypertrophy are dependent on the insulin/IGF1-PI3Kα-Akt axis.

Although pathologic hypertrophic stimuli do not activate this pathway directly, long-term treatment with insulin produces pathologic hypertrophy, associated with increased Akt phosphorylation, as doe's activation of Akt through GPCR-PI3Kγ.

Furthermore, high carbohydrate feeding during pressure overload accentuates pathologic hypertrophy, the degree of which directly correlates with the degree of hyperinsulinemia and increased phosphorylation of Akt.

The transition to pathologic hypertrophy occurs in association with a decrease in capillary density, a feature typical of uremic cardiomyopathy.

In contrast, nuclear-targeted overexpression of Akt1 does not lead to pathologic hypertrophy; instead, hearts display increased numbers of cardiomyocytes, enhanced contractility, and protection from ischemia-reperfusion injury (IRI).

Thus, the insulin-Akt1 pathway is involved in both physiologic and pathologic cardiac hypertrophy. Both the route and context of activation (presence of concurrent stimuli for pathologic hypertrophy) are important in determining which will dominate, as are the duration and subcellular localization of Akt activity.

In the human heart, Akt activity increases as hypertrophy deteriorates into heart failure, although it is not clear whether this is a causal relationship.

Angiogenesis

Physiologic growth of cardiomyocytes is accompanied by increased angiogenesis maintaining capillary density. In experimental and clinical studies of CKD, capillary growth failed to keep pace with myocytes hypertrophy, resulting in decreased density. This effect is not seen in experimental essential hypertension, suggesting it is specific to uremic cardiomyopathy.

Coronary angiogenesis is under the dual control of vascular endothelial growth factor (VEGF) and angiopoietin-2 (Ang-2), both of which are up regulated during short-term cardiac Akt1 overexpression associated with physiologic hypertrophy.

In contrast, after chronic overexpression of Akt1 and consequent pathologic hypertrophy, VEGF and Ang-2 are down regulated in association with reduced capillary density. Furthermore, short-term overexpression of Akt1 produces pathologic hypertrophy when VEGF is inhibited simultaneously, and inhibition of VEGF during pressure overload accelerates the transition to heart failure.

Thus, during chronic experimental Akt1 activation, the stimulus for myocyte growth is maintained, but the stimulus for capillary growth declines, resulting in a drop in myocardial capillary density that contributes to the transition to heart failure. A similar state likely occurs within the uremic heart.

Fibrosis

Cardiac fibrosis in uremia has been recognized since the 1940s and was found in experimental and postmortem studies of CKD.

It is of the reactive type, a consequence of endothelial-to-mesenchymal transition followed by activation and proliferation of new interstitial fibroblasts. Compared with control hearts with a similar degree of hypertension and LVH, the uremic cardiac interstitium demonstrates increased expression of proinflammatory mediators, such as PDGF, with correspondingly increased fibrosis, suggesting renal disease enhances myocardial fibrosis.

This interstitial fibrosis contributes to ventricular stiffness and diastolic dysfunction and cardiac dysrhythmias and may further compromise molecular exchange between cardiomyocytes and capillary bed.

Studies investigating the mechanisms underlying this fibrosis are scarce; however, experimental work implicates signaling through mammalian target of rapamycin (mTOR), a downstream target of Akt.

Although there was no evidence of increased phosphorylation of Akt in these studies, neither specific phosphorylation of Akt1 and Akt2 or Akt activity was determined.

Furthermore, the development of insulin resistance was not determined.

Therefore, although the delineation requires further clarification, fibrosis in CKD is mediated in part by activation of a profibrotic intracellular signaling mechanism involving mTOR.

Furthermore, in a nonuremic model, chronic hyperinsulinemia produced pathologic hypertrophy and fibrosis by activation of a complex network of intracellular pathways, including Akt, whereas the use of peroxisome proliferator–activated receptor γ (PPAR-γ) agonists in models of salt-sensitive hypertension decreased cardiac hypertrophy and fibrosis in association with reduced Akt phosphorylation.

Furthermore, as mentioned already, chronic overexpression of Akt1 can produce cardiac fibrosis associated with LVH.

Thus, although cardiac fibrosis is a feature of the uremic heart, knowledge of the underlying mechanisms is still sparse.

There is direct evidence that downstream targets of Akt are involved, and evidence from nonuremic models confirms that perturbations in Akt signaling induce cardiac fibrosis.

Apoptosis

Outcomes after acute myocardial infarction in CKD remain poor, despite optimal conventional therapy, and experimental studies showed the increased susceptibility to IRI of uremic hearts.

Previous work on IRI demonstrated that cell death occurs through necrosis and apoptosis and that inhibiting apoptosis during reperfusion significantly improves outcomes. Cardiomyocyte apoptosis also plays a causal role in the development of uremic and nonuremic heart failure, whereas inhibiting apoptosis reduces cardiac dysfunction in heart failure.

Maintaining cardiac function requires timely de novo production of ATP; however, the production of ATP is reduced within the uremic heart, as evidenced by a decreased phosphocreatine-ATP ratio.

In addition to uremic heart, this restriction has multiple causes, including decreased oxygen and substrate supply as a result of impaired capillary–myocyte exchange, metabolic remodeling, and alterations in creatine kinase. Compromised ATP synthesis also results in a loss of mitochondrial membrane potential and functional deterioration, resulting in a further decline in ATP production and contributing to the inability of the uremic heart to adapt to hemodynamic alterations, a situation similar to that in the failing human heart.

Mitochondrial damage causes the release of cytochrome c triggering apoptosis and cell death, jeopardizing the survival of remaining cardiomyocytes. The importance of apoptotic cell death in the transition from compensated hypertrophy to heart failure is paramount.

Akt stimulation is a potent antiapoptotic signal, and evidence demonstrates that upregulation of the PI3Kα-Akt pathway, by either administration of insulin/IGF-1 or genetic manipulation, reduces apoptosis and improves functional recovery in the face of IRI. Furthermore, inhibition of the PI3Kα-Akt axis, either chemically or with dominant negative Akt, abrogates this protection.

Targeted disruption of Akt isoforms demonstrates that Akt2 rather than Akt1 confers this antiapoptotic effect. Acute activation of Akt2 is thus antiapoptotic and cardioprotective. Chronic Akt activation does not protect against cell loss from IRI and is in fact detrimental, potentially as a result of Akt-mediated inhibition of PI3K, again highlighting important differences between acute and chronic activation of the Akt pathway.

Metabolic

Under normal conditions, the adult heart displays a preference for oxidation of fatty acids, with 60 to 90% of ATP production resulting from this route and the remaining 10 to 40% from glucose and lactate and a small fraction from ketones however; LVH is associated with down regulation of fatty acid oxidation and up regulation of glucose oxidation.

One explanation for this is a switch to “oxygen efficient” fuels during times of metabolic stress. Although this may be initially compensatory, it may contribute to cardiac injury by lipotoxicity or loss of metabolic flexibility. Certainly, in models of pressure overload hypertrophy, although cardiac basal glucose uptake is increased, insulin-stimulated uptake is impaired.

The mechanism for this involves reduced GLUT4 translocation, rather than changes in GLUT4 or GLUT1 expression. Within the uremic heart, expression of GLUT4 and GLUT1 transporters are also unchanged, although there is also some evidence for a defect in GLUT4 translocation in the early stages of experimental uremic cardiomyopathy; the situation in more advance uremic cardiomyopathy is unknown.

Akt2 regulates glucose influx into cardiomyocytes by increasing translocation of GLUT4 while concurrently decreasing fatty acid oxidation through down regulation of transcription factors, such as PPAR-α and PPAR-γ coactivator-1, which are involved in regulation of fatty acid oxidation.

The net effect of acute Akt2 stimulation is increased glucose and decreased fatty acid oxidation, a beneficial effect during hypoxic conditions; however, once again, the consequences of acute and chronic Akt activation differ, with chronic stimulation increasing basal but significantly blunting insulin-stimulated glucose uptake as a result of decreased GLUT4 expression in insulin-sensitive intracellular vesicles, a picture similar to that seen in hypertrophy with uremia.

Reduced myocardial insulin sensitivity could lead to a decreased ability to increase ATP generation in times of need or alter substrate use to match supply, leaving it susceptible to energy depletion. Furthermore, chronic increases in glucose uptake enhance glucose metabolism through non–ATP-generating pathways, including the oxidative pentose phosphate and hexosamine biosynthetic pathways, both of which contribute to myocardial fibrosis and cell death.

Calcium Cycling

Uremia is associated with depressed cardiac function at the level of the myocyte, independent of gross alterations in cardiac structure, or β-adrenoreceptor desensitization.

Although the underlying mechanism is not fully understood, two groups independently identified prolongation of the calcium transient, without a change in amplitude or rate of sarcoplasmic reticulum calcium release.

Recovery of the calcium transient is dependent on the sarcoplasmic calcium-ATPase (SERCA2a) and the sarcolemma sodium-calcium exchanger. In clinical and experimental studies, the transition from compensated hypertrophy to heart failure was associated with down regulation of SERCA2a expression, which was also seen in experimental uremia.

Consequently, the uremic cardiomyocyte is desensitized to calcium, requiring greater diastolic and systolic intracellular calcium concentrations to maintain contraction.

The delayed recovery of the calcium transient and increased diastolic intracellular calcium may translate into clinical diastolic dysfunction.

The insulin-Akt signaling pathway impinges on calcium cycling at several stages, with the net effect of chronic activation of Akt increasing the size of the calcium transient and thus myocyte contraction.

Akt acts on L-type calcium channels, enhancing calcium influx, and sarcoplasmic reticulum calcium reuptake, increasing expression of SERCA2a and phosphorylation of phospholamban.

Whether these components are direct substrates for Akt is not known; however, the reduced expression of SERCA2a seen in uremia might be predicted by a defect in Akt signaling related to uremic insulin resistance.

The coronary microcirculation and myocardial disease

Chilian proposed an elegant model of the coronary circulation consisting of three anatomically distinct but functionally interlinked compartments.

The proximal compartment consists of large epicardial coronary arteries that function as capacitance vessels and respond to shear forces by endothelial mediated dilatation. The middle compartment consists of pre-arterioles that are characterized by a measurable pressure drop along their length. The distal compartment consists of the intramural arterioles that have diameters <100 μm, have high resting tone and are responsible for the majority of coronary vascular resistance.

They dilate in response to changes in myocardial oxygen consumption. Vasoactive mediators such as adenosine and hydrogen peroxide act directly on these vessels to produce vasodilatation.

Endothelium-dependent mechanisms involving nitric oxide and endothelium derived relaxing factors are also important, with animal studies showing attenuated vasodilatation of the coronary microvasculature when nitric oxide synthesis is inhibited.

Finally, the capillary bed delivers oxygen and substrates to the myocytes. Thus, the coronary circulation matches myocardial oxygen demand with supply via a complex interplay between myogenic tone, metabolic signals, circulating hormones and the intrinsic properties of the endothelium.

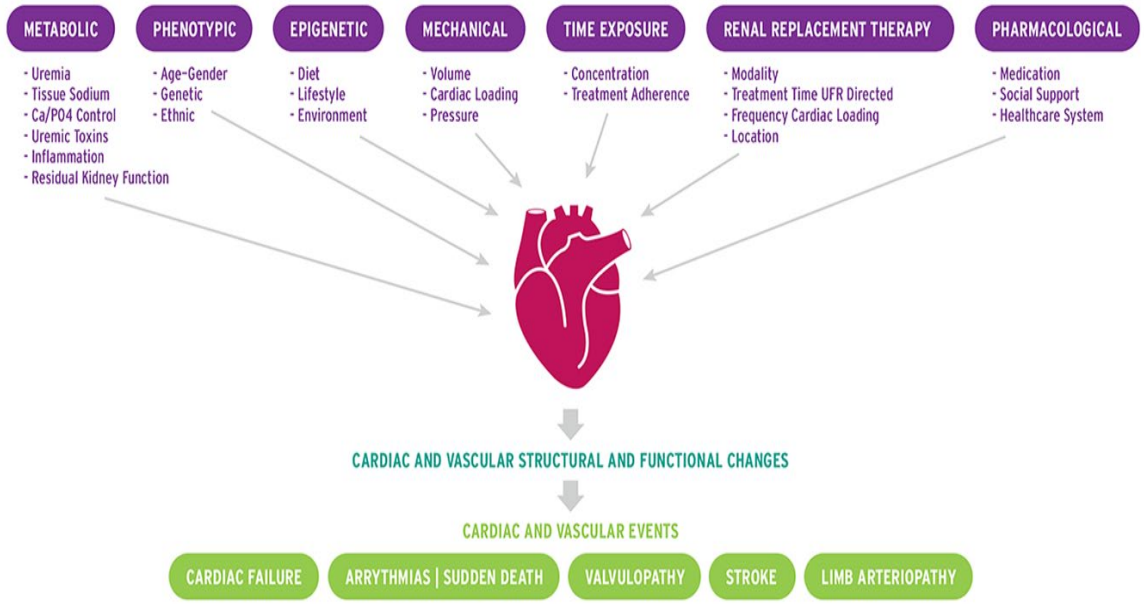
Abnormalities of all of these coronary vessels are seen in uremia with atherosclerosis and medial thickening and calcification of the epicardial vessels, and medial hypertrophy and a reduction in the cross-sectional surface area of the pre-arterioles. Myocyte–capillary mismatch and reduced LV capillary density have also been demonstrated in uremic hearts in both animal models and postmortem human studies.

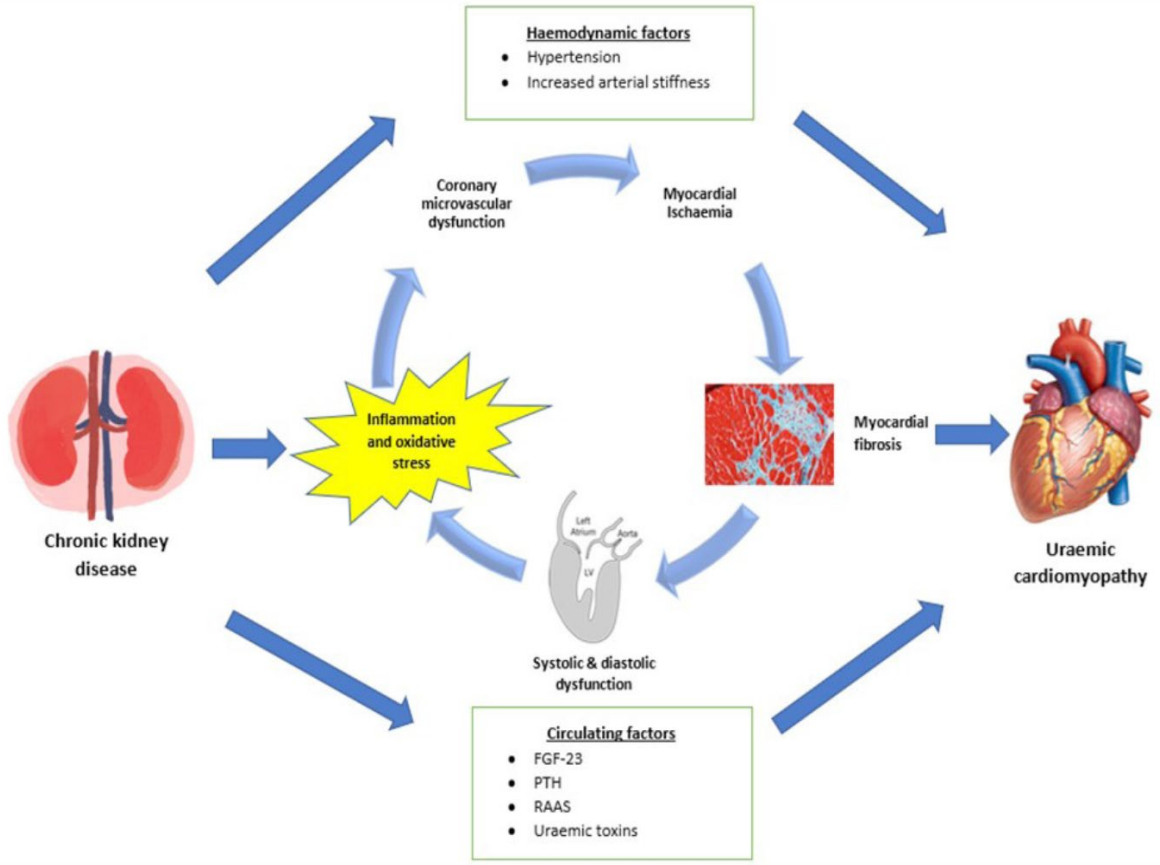
This predicts clinical consequences including reduced LV systolic function, adverse ventricular remodeling, ventricular arrhythmias, clinical heart failure and ***cardiovascular death***.

Similarly in HFpEF, coronary micro vascular dysfunction (CMD) is common with a recent multicenter study identifying CMD in 75% of patients. This was associated with kidney damage, as measured by albuminuria, as well as a higher N-terminal pro-brain natriuretic peptide and systemic arterial dysfunction.

The consequent failure to match myocardial blood flow (MBF) with demand results in widespread ischemia, DIF, ventricular remodeling and systolic and diastolic dysfunction. In CKD, the effect is likely to be exacerbated by hypertension, increased arterial stiffness and humoral factors such as FGF-23 and aldosterone leading to the clinical syndrome of ***uremic cardiomyopathy***.

It is not clear if CMD is the cause or consequence of myocardial disease in uremic cardiomyopathy. However, it is plausible that the relationship between myocardial fibrosis and CMD is reciprocal and a vicious circle is initiated in which both factors exacerbate each other causing progressive ischemia and myocardial dysfunction leading to heart failure, ***arrhythmia and death***.





INSULIN RESISTANCE IN UREMIA AND THE AKT PATHWAY

Insulin resistance is an independent risk factor for cardiac disease in CKD. Early studies demonstrated that insulin resistance in uremia is the result of impaired glucose metabolism unrelated to insulin receptor or GLUT4 transporter function.

The metabolic acidosis seen in CKD is partially responsible for uremic insulin resistance, because the insulin sensitivity of glucose metabolism is improved by correcting pH.

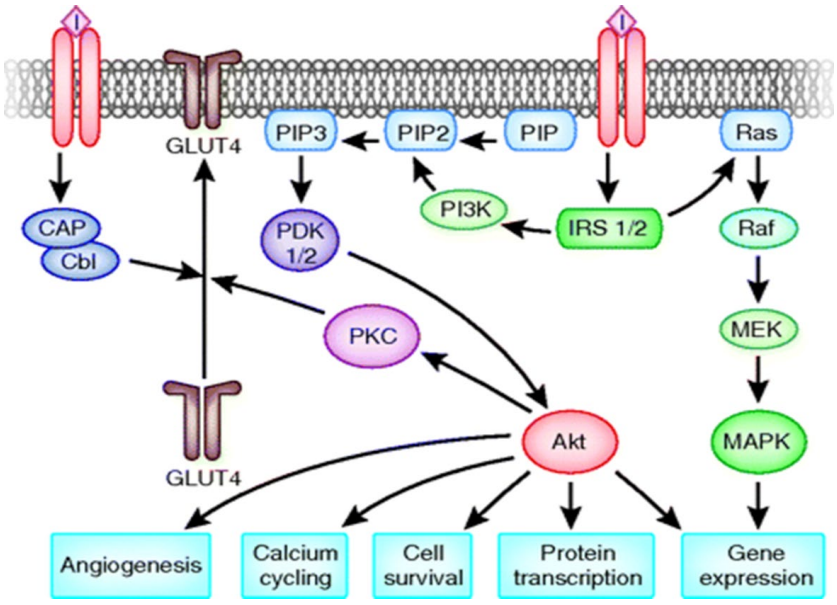
Dialysis therapy also partially corrects insulin resistance, although resistance is still observed in 33% of patients who receive renal replacement therapy. Serum is capable of inducing insulin resistance, suggesting a role for dialyzable toxins, potentially carbamylated amino acids, which produce a post receptor defect in glucose uptake in rats similar to that observed in patients with insulin resistance.

Although insulin resistance associates with impaired signal transduction along the pathway regu-

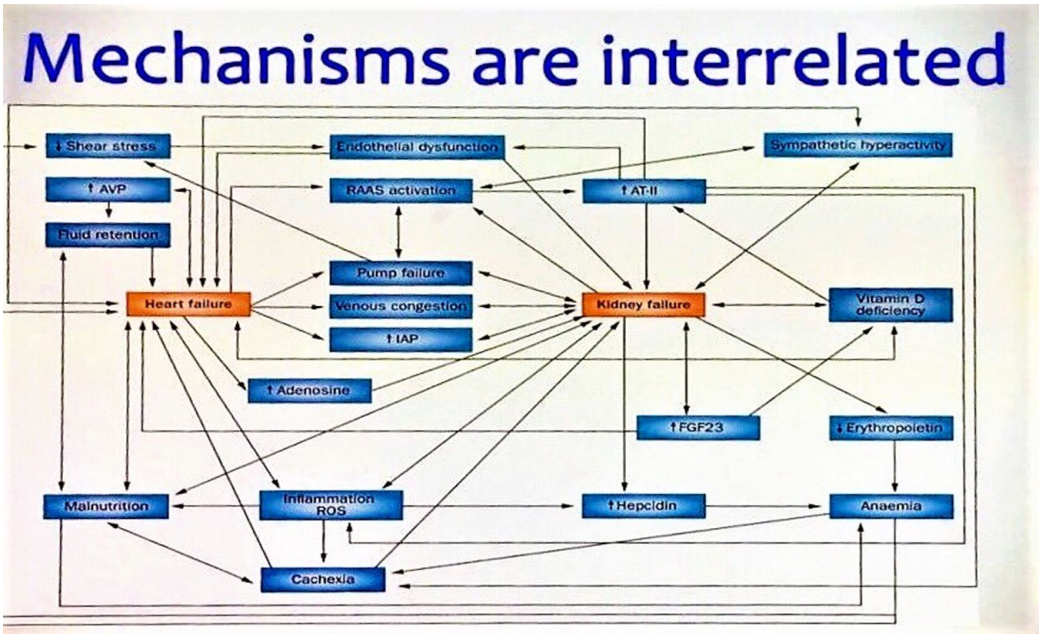
lating insulin-mediated glucose uptake, clinical and experimental studies show intact insulin signaling along paths regulating some of insulin's pleiotropic actions (Figure 1).

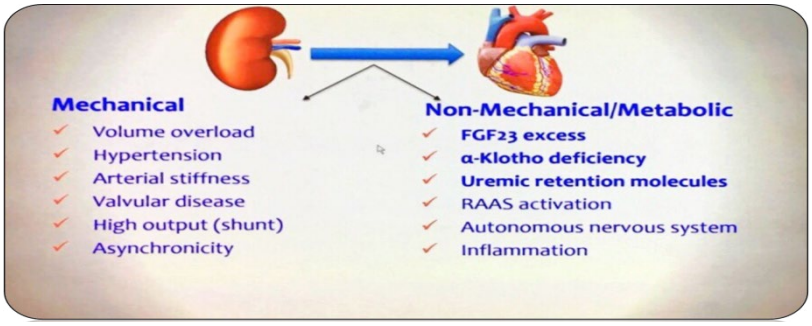
The reactive hyperinsulinemia of insulin resistance, necessary to maintain serum glucose, may lead to up regulation of these effects. These disturbances in the effects of insulin are fundamental to the negative consequences of insulin resistance.

Akt acts as a focal point for the dispersion of post receptor signal among many of pleiotropic effector pathways of insulin, and although perturbations in Akt activity have been identified in many models of hypertrophic cardiac disease, its characterization in the uremic heart remains incomplete.



Simplified schematic demonstrating the three principle arms of intracellular insulin signal transduction: The CAP-Cbl lipid raft, the PI3K-Akt axis, and the mitogen-activated protein kinase (MAPK) system. Akt can be seen to hold a pivotal point in distribution of the signal to the effectors of the pleiotropic actions of insulin.





AKT SIGNALING PATHWAY

Akt, known previously as protein kinase B, is a serine/threonine protein kinase with homology to protein kinase A and protein kinase C. Three isoforms of Akt exist in mammals (Akt 1 through 3), although in the heart, Akt1 and Akt2 predominate.

In resting cells, Akt resides in the cytosol, and stimulation of either PI3Kα, through insulin or IGF-1, or PI3Kγ, through G-protein–coupled receptors, leads to generation of phosphatidylinositol-3,4,5-trisphosphate and recruitment of Akt to the plasma membrane (Figure 2).

There, Akt is phosphorylated at two regulatory sites by phosphoinositide-dependent kinases 1 and 2, respectively.

Phosphorylation of both regulatory sites is required for full activation of Akt, which has a number of intracellular targets (Figure 2).

The consequences of Akt activation vary greatly depending on the route of activation and its duration and the specific isoform affected. For example, in normal health, insulin-PI3Kα-Akt signaling induces physiologic hypertrophy, yet insulin-stimulated Akt activity also augments pathologic hypertrophy in the context of pressure overload; Akt activation through G-protein–coupled receptors and PI3Kγ results in pathologic hypertrophy.

Furthermore, whereas Akt1 is the dominant isoform implicated in regulation of postnatal cardiac growth, Akt2 plays the dominant role in coronary angiogenesis, glucose metabolism, and cell survival. It is this variation that makes Akt such a vital signaling component.

Schematic representation of Akt activation. Simplified representation of Akt activation by PI3K.

Akt is recruited to the plasma membrane by PIP3, allowing phosphorylation of two control sites (Thr308 and Ser473), by phosphoinositide-dependent kinase 1 (PDK1) and PDK2.

Dephosphorylation of PH domain by protein phosphatase 2a (PP2A) and leucine-rich repeat protein phosphatases (PHLPP). HM, KD, and PH represent domains of Akt.

AKT SIGNALING IN UREMIA

The integrity of Akt signaling in the uremic state is not fully elucidated; there are no clinical data and only incomplete experimental information. In one model of CKD, total Akt was suppressed after 3 months of uremia, but phosphorylated Akt was not assessed.

Another study demonstrated increased Akt phosphorylation but did not determine total Akt expression.

Neither study directly assessed Akt activity or determined the relative expression or activity of Akt1 and Akt2; however, it is apparent that uremia causes significant perturbations in the Akt system.

In patients with diabetes and models of insulin resistance, inhibition of insulin-stimulated Akt2 activity is seen, but Akt1 activity is preserved. As described in the next section, this imbalance of Akt1 and Akt2 activity predicts a cardiac phenotype very similar to that seen in the uremic heart.

DIAGNOSIS

Invasive coronary angiography

CFR can be assessed during invasive coronary angiography. Two different methods exist but both expose patients to infrequent but significant risks including vascular injury, contrast nephropathy and death.

Doppler guide wire

An angioplasty wire tipped with a high frequency piezoelectric Doppler transducer can be used to measure flow velocities in a coronary artery at rest and at hyperemia. CFR is calculated as the ratio of hyperemic/resting flow.

Intracoronary thermo dilution

CFR can be accessed via thermo dilution. A pressure wire is positioned in the distal third of a target vessel. The shaft of the pressure wire acts as a proximal thermistor while the sensor at its tip acts as a distal thermistor.

Positron emission tomography

The non-invasive ‘gold-standard’ method of assessing CFR is quantitative PET. Absolute values of MBF at rest and during hyperemia can be calculated.

MRI

MRI is emerging as a useful tool for the non-invasive assessment of CFR, although it remains less validated than other imaging modalities. Methods include:

Coronary sinus flow

The majority of blood from epicardial ventricular veins drains into the coronary sinus, which can be visualized on MRI using velocity encoded cine sequences. CFR is the ratio of blood in the coronary sinus after hyperemia compared with baseline.

First pass perfusion

Myocardial perfusion is recorded in dedicated basal, mid-ventricular and apical short axis slices at rest and during stress. The ratio of the maximal upslopes of signal intensity during vasodilatation over resting condition is defined as myocardial perfusion reserve. Perfusion defects can be identified to help localize coronary artery lesions and assessments of viability can be made using late gadolinium enhancement. However, the need for gadolinium limits its utility in CKD.

Stress T1 mapping

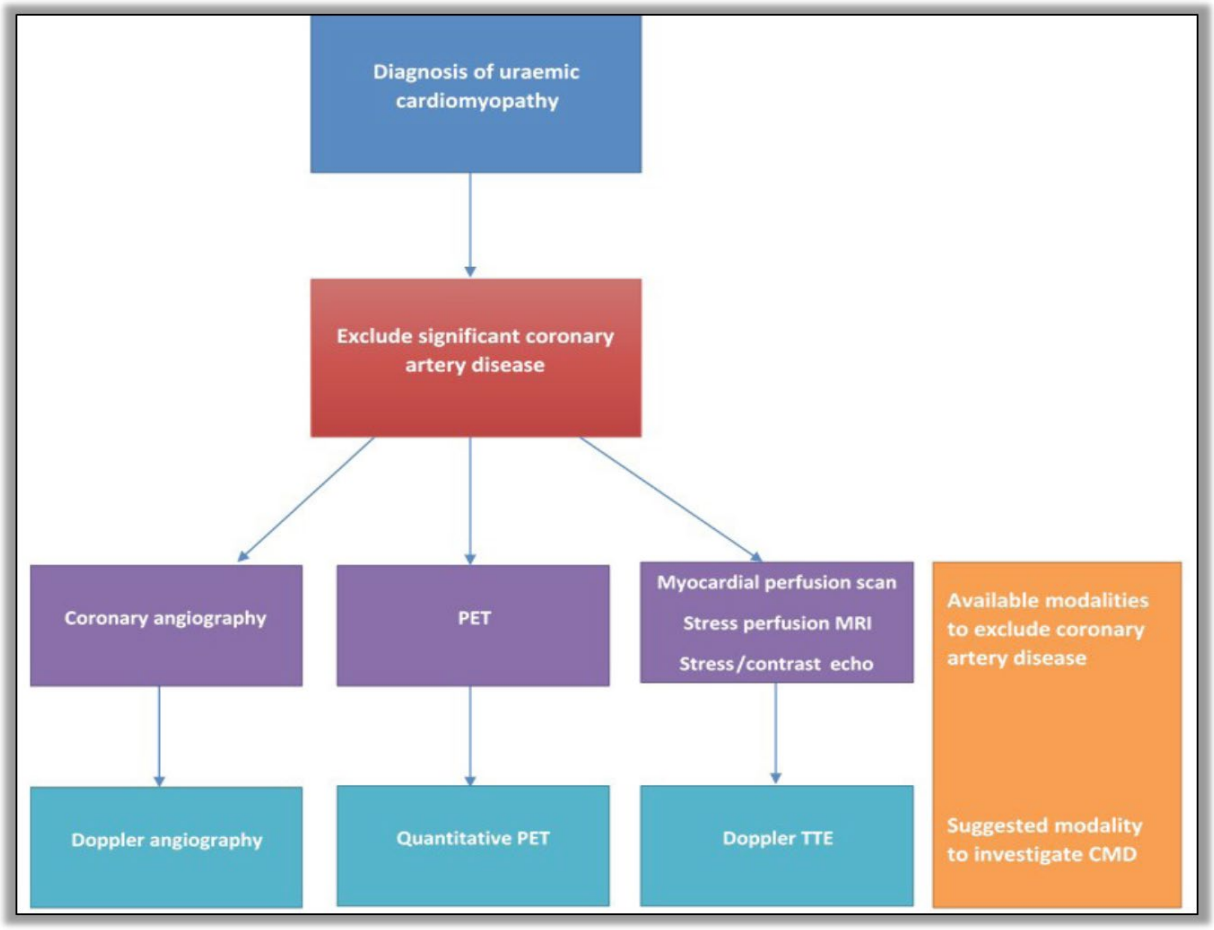
T1 relaxation times of tissues are prolonged by increased water content. Coronary vasodilatation, by increased myocardial blood volume, would be expected to prolong T1 times. Using this principle, measurement of rest and stress T1 times provide an indirect indication of increased MBF and myocardial perfusion reserve.

Doppler transthoracic echocardiography

CFR can be measured using Doppler transthoracic echocardiography (TTE) and correlates well with invasive Doppler and PET. The mid to distal left anterior descending artery (LAD) can be identified in a modified apical two-chamber view using a high frequency transducer and appropriate machine settings to identify low velocity flow. Pulse wave Doppler signals can be measured in the LAD at rest and during hyperemia to calculate CFR.w14 This technique is feasible in most patients, including those who are obese, as it is less reliant on good acoustic windows due to the superficial location of the LAD.

Myocardial contrast echo

Myocardial contrast echocardiography uses protein micro bubbles that have a lower diameter than the red blood cell, resist arterial pressure and remain intravascular in the intact circulation. These qualities enable direct quantification of micro vascular perfusion and allow absolute MBF as well as CFR to be calculated.



Conclusions:

1. LVH is present from the earliest stages of progressive renal disease. This, and other forms of uremic cardiomyopathy, is linked to increased QT interval and dispersal, and with minor rhythm abnormalities, providing a link with the high risk of sudden death.
2. CMD provides a plausible mechanism by which factors associated with impaired kidney function, including oxidative stress and inflammation, might result in myocardial damage and dysfunction leading to the syndrome of uremic cardiomyopathy.
3. Current data on CMD in uremic cardiomyopathy are limited and conflicting, hampered .by the retrospective design of most studies. Consequently, there is a need for well-designed prospective studies of CMD in CKD, to identify whether CMD might be a key mediator in the development of uremic cardiomyopathy.

4. The so-called “uremic” cardiomyopathy is heterogeneous (systolic and diastolic dysfunction) and multi-factorial. The term “uremic” is somewhat deceptive because it suggests that all cardiac abnormalities are related to uremic toxicity.
5. In reality, uremic cardiopathy depends largely on non-specific and potentially reversible factors such as anemia, hypertension and over hydration. It is the association and long-term persistence of these factors that are relatively specific to uremia.

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РЕЗЮМЕ

УРЕМІЧНА КАРДІОМІОПАТІЯ

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Вступ. Хронічна хвороба нирок (ХНН) є поширеною, вражаючи кожного сьомого західного населення. Існує добре задокументована зворотна залежність між серцево-судинним ризиком і швидкістю клубочкової фільтрації (eGFR), яка не залежить від віку, статі та інших факторів ризику.

Мета. Навести сучасні дані літератури про уремічну кардіоміопатію.

Матеріали та методи. Огляд сучасних та зарубіжних літературних джерел; методи – опис, аналіз, реферування.

Результати та їх обговорення. У роботі детально описані хронічна хвороба нирок, уремічна кардіоміопатія, причини, патогенез, ускладнення.

Висновки. Уремічна кардіоміопатія значною мірою залежить від неспецифічних і потенційно оборотних факторів, таких як анемія, гіпертонія та надмірна гідратація. Саме асоціація та довгострокова стійкість цих факторів є відносно специфічними для уремії.

Ключові слова: аритмія, трансплантація, артеріальна гіпертензія, гіпертрофія лівого шлуночка, діаліз, хронічна ниркова недостатність, інтервал QT.

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