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New Perspectives of Nephropathies

K. Gazdíková (Katarína Gazdíková)[1], J. Deglovič (Juraj Deglovič)[2]

Summary

Mitochondria are intracellular organelles involved in several key biological processes in the cell, including energy production, redox signaling, homeostasis, inflammation, aging, innate immune response, and mitophagy. Mitochondrial functional defects play an important role in the pathogenesis of diseases of kidneys such as tubular diseases, interstitial nephritis, focal and segmental glomerulosclerosis, and diabetic nephritis. In addition, participation in the pathogenesis of nephrotoxicity and carcinogenesis. Supplementation with CoQ_{10} results in the correction of e.g. neurological symptoms. For kidney diseases, results are so far controversial. Combined with vitamin C and carnitine, as an artefactual electron acceptor and cofactor, they showed a partial positive effect.

Keywords mitochondria, mitochondrial nephropathy, diabetic nephropathy, chronic kidney diseases, acute kidney injury, glomerulonephritis, coenzyme Q 10

[1)] Slovak Medical University, Institute of General Medicine of Faculty of Medicine

[2)] Slovak Medical University, Institute of Dentistry of Faculty of Medicine

Correspondence to

Katarína Gazdíková
Slovak Medical University,
Institute of General Medicine of Faculty of Medicine
Limbova 12
833 01 Bratislava
Slovak Republic

katarina.gazdikova@szu.sk

Reviewers

Dr. Daniel J. West, Jr.

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Introduction

Kidneys are vital paired organs that perform three basic functions: excretory - secretory, metabolic and endocrine.

The kidneys undergo processes aimed at the excretion of nitrogenous substances and fluids in order to maintain homeostasis, which require sufficient energy, making the kidneys one of the most metabolically and energetically demanding organs with the need for sufficient numbers (especially in the proximal tubules) as well as for the proper functioning of the mitochondria (MITO) [1,2]. Although the key role of MITO is energy and adenosine triphosphate (ATP) production, in the kidney they also regulate apoptosis, steroid synthesis, calcium (Ca), iron (Fe) homeostasis as well as other processes [3].

Energy supply from renal MITOs is dependent on lipid metabolism with β-oxidation of fatty acids (FAs) and the Krebs cycle. Renal MITOs integrate several metabolic pathways ensuring maintenance of energy homeostasis for both static and dynamic demands [2]. The formation of energy from glucose is accomplished by 2 pathways, namely glycolysis in the cytoplasm and oxidative phosphorylation (OXPHOS) in the MITO. OXPHOS is the most efficient energy producer, generating more than 36 ATP from a single molecule of glucose compared to only 2 ATP molecules generated by glycolysis. In addition, it can utilize all the nutrients available to the cells. Structural damage and dysfunction of MITO are considered to be one of the important factors in the development of acute and chronic kidney diseases [4].

Mitochondrial damage and kidney disease

MITOs contribute to ROS free radical production and the transmission of metabolic and stress signals [5]. A common feature for all forms of acute and

chronic kidney injury is the toxic ROS and RNS present at disease manifestation. This oxidative stress-conditioned damage is caused by ischemia/reperfusion, energy deficiency conditioned by impaired MITO biogenesis or ATP energetics, or defective clearance of damaged MITO by mitophagy. All of these processes cause immune cell activation, accumulation of inflammatory cytokines, apoptosis and tissue damage. The phenotypic manifestations of MITO dysfunction in the kidney are proximal tubule dysfunction, tubulointerstitial disease, cystic kidney disease, podocytopathy and nephrotic syndrome. All renal diseases also increase cardiovascular (CV) morbidity and mortality [6].

MITO dysfunction plays an important role in the pathogenesis of several renal diseases in the early stages, as well as in the progression of kidney disease [7)], including acute kidney injury (AKI) and chronic kidney diseases (CKD) [8, 9].

Acute kidney diseases and mitochondrial damage

MITOs play a dual role in AKI - they are the primary source of energy for each cell and are also a key regulator of cell death. Even minor AKI can progress to fibrosis and subsequently to ESRD. Several studies have shown that it is the fitness of MITOs that is the major determinant in the pathogenesis in restoring function. Impairment of MITO function early in the course of AKI is a key factor leading to tubular damage and persistent renal insufficiency. AKI is accompanied by functional and structural changes in MITO (Figure 1) [10].

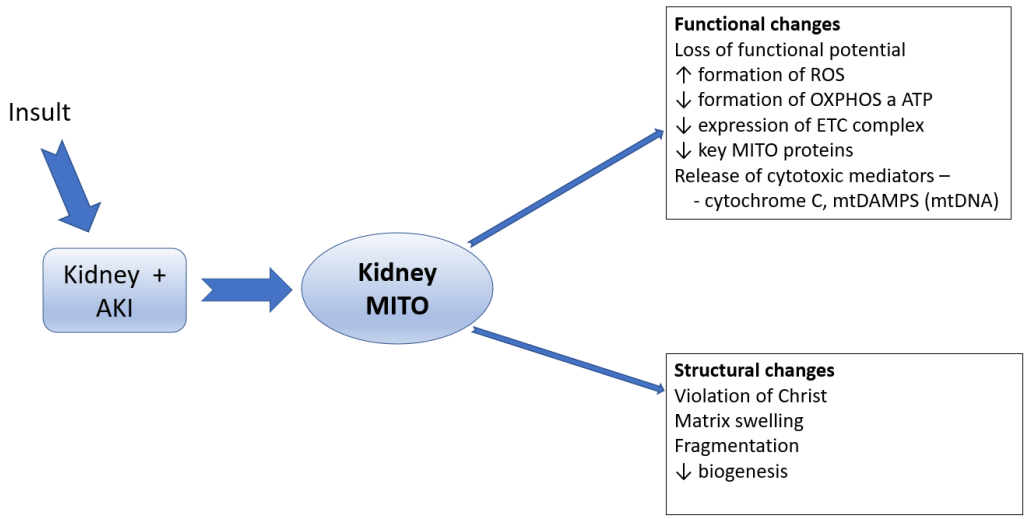


Figure 1 Mitochondrial structural and functional changes during AKI (modified from [10])

Chronic kidney diseases and mitochondrial disease

CKD is structural or functional kidney damage with a tendency to progression or complications due to reduced glomerular filtration, lasting more than 3 months, affecting health status. CKD is not a distinct diagnosis, but is a generic name for heterogeneous disorders of renal structure and function with different clinical manifestations. Renal impairment is now most often secondary to other underlying so-called diseases of civilization, such as diabetes mellitus (DM) and arterial hypertension (AH). AH, DM and obesity play a significant role in the pathogenesis of MITO injury [11)]. In most patients, it is asymptomatic for a long time and is therefore often diagnosed only in

advanced stages [12]. Worldwide, the prevalence of all stages of CKD is reported to be 9-13%, i.e. 850 million people [13, 14].

Both obesity and metabolic syndrome accelerate the progression of CKD and exacerbate CKD-dependent sarcopenia. Both conditions are associated with renal alterations in energy metabolism and lower tissue ATP levels and secondarily lead to MITO dysfunction and reduced MITO numbers [15].

Uremic toxins accumulated in AKI and CKD induce MITO damage and, in turn, MITO damage itself exacerbates renal damage, creating a vicious cycle of CKD progression (Fig. 2) [11]. MITO damage is accompanied by morphological changes leading to ROS accumulation with initiation of inflammation, cyto C release resulting in apoptosis, or deficient ATP production leading to cell damage [11].

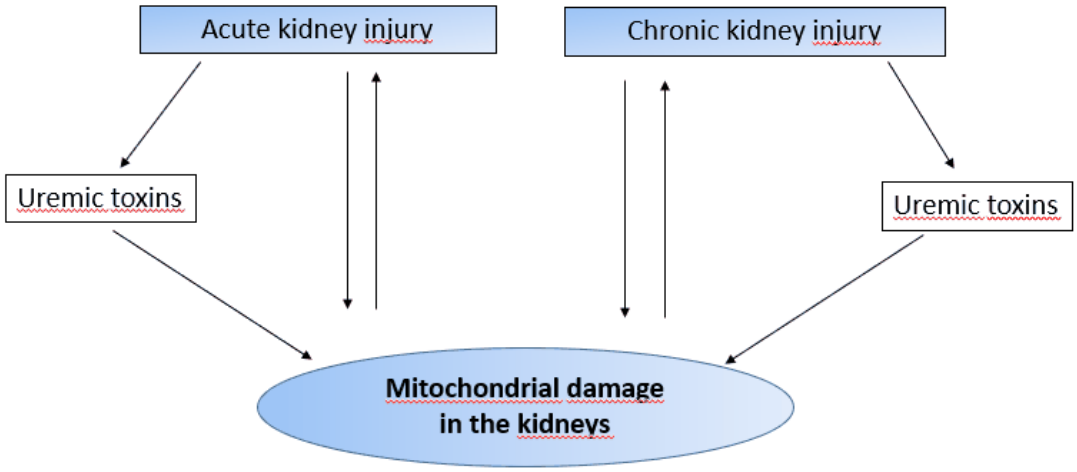


Figure 2 Mitochondrial damage in acute kidney injury and chronic kidney disease (modified from [11])

Dysregulation of MITO homeostasis, changes in bioenergetics as crosstalk with organelle stress contribute to the transition of AKI to CKD [11]. The mechanism of this transition is not yet fully elucidated, but their causal relationship is undoubted (Fig. 3) [16].

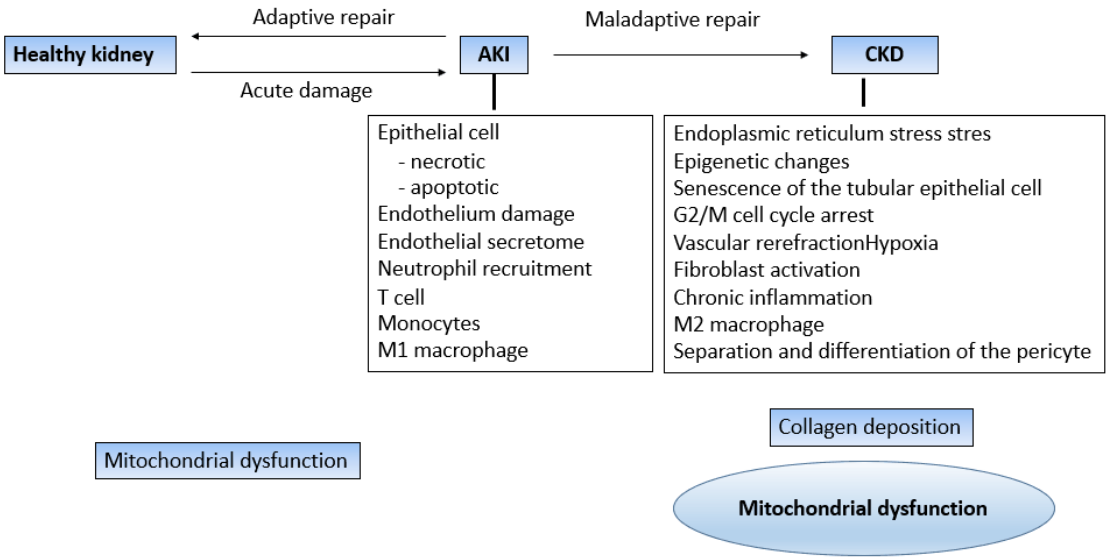


Figure 3 Pathophysiological processes in the continuum of acute kidney injury to chronic kidney disease (modified from [16])

Legend: mtDAMPs - mitochondrial damage-associated molecular patterns

Currently, AKI and CKD are considered to be two poles of the same disease. As mentioned above, MITO aberrations play an important role in both promoting glomerular and tubulointerstitial inflammation and tubulointerstitial fibrosis.

Diabetic nephropathy and mitochondria

In Europe, the USA and most countries in the world, DM is now the most common cause of ESRD with a proportion of around 40%. Moreover, CKD, like DM, is a significant CV risk factor and the combination of both significantly worsens the overall prognosis of the patient [14].

DN is defined as a clinical syndrome arising from long-term specific renal morphological and functional changes in patients with DM of all types. It develops because of diabetic metabolic disorder, mainly chronic hyperglycaemia. It is manifested by proteinuria, renal hypertrophy, renal fibrosis with a progressive decline in renal function. Genetic predisposition is also involved in the manifestation of DN.

The pathogenesis of DN is multifactorial, involving all 4 renal components - glomeruli, tubules, interstitium and vessels. Chronic hyperglycaemia is the initial cause, which, together with the accrual of pathological intrarenal mechanisms, leads to pathological functional and structural changes in all parts of the nephron. There is endothelial dysfunction, thickening of the glomerular basement membrane, disruption of podocyte function with consequent increased albumin permeation into tubular structures and their damage. The intrarenal activity of the renin-angiotensin-aldosterone system (RAAS) is increased with intraglomerular hypertension with hyperfiltration in the glomeruli, potentiating glomerulosclerosis. The production of growth and pro-inflammatory factors is also increased, with proliferation in the mesangium. Polygenetic factors play an important role in the etiology of DN.

There is also evidence of a significant impact of the often-present anaemia (hypoxia, aggravation of interstitial fibrosis), which increases the risk of DN progression and can be slowed by its treatment (erythropoietin) [12]. Aberrant MITO homeostasis also plays a key role in the progression of DN [17].

Hyperglycemia induces overproduction of ROS OS, disrupts MITO-glutathione transport, increases MITO activation of ubiquitous NAD(P)H oxidase 4 (NOX4) in the respiratory chain, decreases the stability of mtDNA against ROS production, apoptosis of podocytes, leading to cell damage with fatal diabetic complications [6].

Good glycaemic control is the best preventive measure against the development of DN. DM-induced MITO dysfunction includes abnormal mitophagy, fission, fusion and biosynthesis. If MITO dysfunction is not restored, renal function may continue to decline as DN progresses [18, 19].

Glomerulonephritis and mitochondria

Chronic glomerulonephritis (GNF) is an immune-mediated inflammation of the glomeruli with subsequent changes in other renal structures leading to haematuria, proteinuria, AH and oedema. They represent approximately 10% of all causes of CKD. Congenital GNFs can be caused by mutations of MITO proteins. The abnormal shape of MITO is already present before disease progression to secondary or acquired focal segmental glomerulosclerosis (FSGS), a severe form of GNF. In an animal mouse model, disruption of MITO autophagy is responsible for FSGS [6].

4. Coenzyme Q 10 and kidneys

CoQ_{10} is an essential fat-soluble substance found in all cell membranes. The main antioxidant (AO) role of CoQ_{10} is direct protection against lipid peroxidation and interaction with α-tocopherol. In humans, its positive effect is manifested in efficient MITO energy metabolism and protection against MITO dysfunction, rather than its direct cellular AO effect. Supplementation with CoQ_{10} results in the correction of e.g. neurological symptoms. For kidney diseases, results are so far controversial. Combined with vitamin C and carnitine, as an artefactual electron acceptor and cofactor, they showed a partial positive effect.

The standard recommendation for MITO nephropathies is the administration of CoQ_{10} in combination with vitamin E and vitamin C, which, in addition to nephrological symptomatology, also affect the overall MITO disability [4].

Increased lipid peroxidation (MDA) and decreased CoQ_{10} levels have been shown to be proportional to the decline in renal function [20, 21] in patients with CKD underlying TIN. Similar results were confirmed in CKD patients in the predialysis phase as well as in dialysis patients. CoQ_{10} supplementation not only led to an effect on OS and inflammation in HD patients, but also reduced the development of CV disease in CKD patients [21].

In our clinical follow-up of the effect of CoQ_{10} at a dose of 240mg/day of CoQ_{10} - Q-GEL™ FORTE, vitamin E and C at 1mg/day, and riboflavin 30mg/day in patients with nephropathies, there was a modification of AO capacity (Table 1) [20, 21]. CoQ_{10} levels were optimized, and lipid peroxidation was reduced (decrease in MDA levels). There were no statistical differences in creatinine clearance, creatinine levels. Tubular renal function did not change statistically significantly during follow-up. However, decreases in fractional excretion of α-amino nitrogen and increases in urinary ammonia excretion were noted in some patients. No changes in lipid parameters were observed, although there was a positive trend in very low-density lipoprotein (VLDL) levels as well as an overall tendency for lipid parameters to correct

TABLE 1 EFFECT OF ANTIOXIDATIVE THERAPY ON LEVELS OF SELECTED ANTIOXIDANTS AND LIPID PEROXIDATION [21]

Month 0 1 2 3
Plasma
CoQ_{10} (μmol/l) 0,15±0,04 * 0,21±0,04 1,39±0,15 1,79± 0,15
α-tocopherol (μmol/l) 32,15±4,73 47,15±6,42 56,43±9,72 44,83±5,82
β-carotene (μmol/l) 0,25±0,07 0,30±0,04 0,34±0,08 0,56±0,02
MDA (μmol/l) 5,26 ±0,2 4,95±0,17 5,23±0,16 5,22 ±0,08
Blood
CoQ_{10} (μmol/l) 0,11±0,03 0,20±0,03 1,44±0,18 1,66± 0,16

Notes: CoQ_{10} – coenzyme k Q_{10}, MDA – malondiladehyde, *average±SEM

Conclusion

MITO plays a crucial role in many kidney pathologies including AKI, CKD, DN, GNF. Recognition, diagnosis and treatment of MITO dysfunctions are in the interest of several scientific teams. Causal treatment of genetic defect-induced MITO dysfunctions is currently mostly limited to laboratory conditions [4, 22].

REFERENCES

1. BHATIA, D.; CAPILI, A.; CHOI, M.E. Mitochondrial dysfunction in kidney injury, inflammation, and disease: potential therapeutic approaches. *Kidney Res Clin Pract* **2020**, *39(3)*, 244-258, https://doi.org/10.23876/j.krcp.20.082.

2. LIN, P.H.; DUANN, P. Dyslipidemia in kidney disorders: Perspectives on mitochondria homeostasis and therapeutic opportunities. *Front. Physiol.* **2020**, *11:1050*, https://doi.org/10.3389/fphys.2020.01050.
3. PLOTNIKOV, E.; CIARIMBOLI, G. Editorial: Mitochondria in renal health and disease. *Front. Physiol.* **2021**, *12:707175*, https://doi.org/10.3389/fphys.2021.707175.
4. GAZDÍKOVÁ, K.; FOJTOVÁ, A.; TICHÁ, L. Kidney manifestation of mitochondrial disorders. *Bratisl Lek Listy* **2022**, *123(9)*, 659-671, https://doi.org/10.4149/bll_2022_106.
5. FLEMMING, N.B.; GALLO, L.A., FORBES, J.M. Mitochondrial dysfunction and signaling in diabetic kidney disease: oxidative stress and beyond. *Semin Nephrol* **2018**, *38(2)*, 101–110, https://doi.org/10.1016/j.semnephrol.2018.01.001.
6. PU, D.; PEI-HUI, L. Mitochondrial damage and kidney disease. *Adv Exp Med Biol* **2017**, *982*, 529-551, https://doi.org/10.1007/978-3-319-55330-6_27.
7. BHARGAVA, P.; SCHNELLMANN, R.G. Mitochondrial energetics in the kidney. *Nat Rev Nephrol* **2017**, *13(10)*, 629–646, https://doi.org/10.1038/nrneph.2017.107.
8. AL DALBHI, S.K.; ALQARNI, F.A.; BAHATHEQ, N.M.; ALRASHEED, R.S.; ALKHOWAITER, R.A.; ALNUGHAIMSHI, A.A. Mitochondrial dysfunction and kidney disease. *J Nephropathol* **2019**, *8(2)*, e18, https://doi.org/10.15171/jnp.2019.18.
9. MISE, K.; GALVAN, D.K.; DANESH, F.R. Shaping Up Mitochondria in Diabetic Nephropathy. *Kidney* **2020**, *3601(9)*, 982–992, https://doi.org/10.34067/kid.0002352020.
10. Li, Y.; Hepokoski, M.; Gu, W.; Simonsom, T.; Singh, P. Targeting mitochondria and metabolism in acute kidney injury. *J Clin Med* **2021**, *10(17)*, 3991, https://doi.org/10.3390/jcm10173991.
11. TAKEMURA, K.; NISHI, H.; INAGI, R. Mitochondrial dysfunction in kidney disease and uremic sarcopenia. *Front Physiol* **2020**, *11*, 565023, https://doi.org/10.3389/fphys.2020.565023.
12. GAZDÍKOVÁ, K. Choroby obličiek v ambulancii v8eobecného lekára. In *Gazdíková a kol. V8eobecné lekárstvo*, vydanie prvé; Solen: Bratislava, Slovenská republika, 2021; s. 1069-1128, ISBN 978-80-89858-23-1.
13. KDIGO 2021 Clinical practice guideline for the management of blood pressure in chronic kidney disease. *Kidney Int* **2021**, *99(Suppl 3)*, S1–S87, https://doi.org/10.1016/j.kint.2020.11.003.
14. OK7A, A.; SCHNORER, Z.; RA7LOVÁ, K.; MARTINKA, E.; ULIČIANSKY, V. Diabetická nefropatia – chronická choroba obličiek pri diabetes mellitus: diagnostika, prevencia a liečba. Odporúčané postupy Slovenskej nefrologickej spoločnosti a Slovenskej diabetologickej spoločnosti – UPDATE 2021. *Diab Obez* **2021**, *64(Supplementum)*, 5–13, https://www.diabetesaobezita.sk/casopisy/diabetes-a-obezita/2021-supplementum/diabeticka-nefropatia-chronicka-choroba-obliciek-pri-diabetes-mellitus-diagnostika-prevencia-a-liecba-127219.
15. ANDRES-HERNANDO, A.; LANASPA, M.A.; KUWABARA, M.; ORLICKY, D.J.; CICERCHI, CH.; BALES, E.; GARCIA, G.E.; RONCAL-JIMENEZ, C.A.; SATO, Y.; JOHNSON, R.J. Obesity causes renal mitochondrial dysfunction and energy imbalance and accelerates chronic kidney disease in mice. *Am J Physiol Renal Physiol* **2019**, *317(4)*, F941–F948, https://doi.org/10.1152/ajprenal.00203.2019.
16. JIANG, M.; BAI, M.; LEI, J.; XIE, Y.; XU, S.; JIA, Z.; ZHANG, A. Mitochondrial dysfunction and the AKI-to-CKD transition. *Am J Physiol Renal Physiol* **2020**, *319(6)*, F1105- F1116, https://doi.org/10.1152/ajprenal.00285.2020.
17. SHARMA, K. Obesity and diabetic kidney disease: role of oxidant stress and redox balance. *Antioxid Redox Signal* **2016**, *25(4)*, 208–216, https://doi.org/10.1089/ars.2016.6696.
18. MIMA, A. Mitochondria-targeted drugs for diabetic kidney disease. *Heliyon* **2022**, *8(2)*, e08878, https://doi.org/10.1016/j.heliyon.2022.e08878.
19. FLEMMING, N.; PERNOUD, L.; FORBES, J.; GALLO, L. Mitochondrial dysfunction in individuals with diabetic kidney disease: A systematic review. *Cells* **2022**, *11(16)*, 2481, https://doi.org/10.3390/cells11162481.
20. GAZDÍKOVÁ, K.; GVOZDJÁKOVÁ, A.; KUCHARSKÁ, J.; SPUSTOVÁ, V.; BRAUNOVÁ, Z.; DZÚRIK, R. Oxidative stress and plasma concentrations of coenzyme Q10, alpha-tocopherol, and beta-carotene in patients with a mild to moderate decrease of kidney function. *Nephron* **2001**, *88(3)*, 285, https://doi.org/10.1159/000046007.
21. GAZDÍKOVÁ, K.; GVOZDJÁKOVÁ, A.; KUCHARSKÁ, J.; DZÚRIK, R. Vplyv vybraných antioxidantov na lipidové parametre u konzervatívne liečených pacientov s chorobami obličiek. *Aktuality v nefrologii* **2001**, *7*, 10-13, ISSN 1210-955X.
22. GAZDÍKOVÁ, K.; MOJTO, V. Mitochondrial nephrology. In *Gvozdjáková, A., Cornéllisen, G., Singh, R.B. Recent Advances in Mitochondrial Medicine and Coenzyme Q10*. Nova Science Pub Inc: New York, USA, 2018; 155-186, ISBN: 978-1-53613-149-9.