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Editorial

Novel Nonsteroidal Mineralocorticoid Receptor Antagonists a Promising Strategy for Chronic Kidney Disease Patients and Diabetic Nephropathy

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The story of mineralocorticoid receptor antagonists (MRAs) started initially with 'aldosterone antagonists (AAs)' as the report of the first AAs during the 1950s being encouraged by identifying inhibitors aldosterone activity in animals and humans.

The 60 years of MRA research and progress was a journey with three waves. It started with the identification of steroid-based spironolactone as the first anti-mineralocorticoid, shortly after the purification of aldosterone. Continued with the discovery of more specific steroidal anti mineralocorticoids. And in the last two decades, we are facing the ultimate goal of identifying novel nonsteroidal MRAs with individualized pharmacokinetic and pharmacodynamic qualities for use as safe and efficacious drugs for a broad spectrum of diseases [1].

The third and fourth-generation MRAs share a nonsteroidal structure, where finerenone and esaxerenone are currently being evaluated in clinical trials, while no clinical data are available for apararenone. Finerenone is thought to have higher potency and less rick for hyperkalemia than steroidal MRAs such as spironolactone and eplerenone due to the differential distribution of the drug in the heart and kidney [2]. The renal elimination of finerenone is minimal, although in moderate and severe renal impairment, there is increased exposure to unbound finerenone by 57% and 47%, respectively, possibly due to renal impairment and nonrenal routes of elimination [3].

Inappropriate activation of the mineralocorticoid receptor (MR) plays a crucial role in the development of hypertension, cardiovascular disease (CVD) and chronic kidney disease (CKD).

The adrenal cortex's primary stimuli for aldosterone synthesis and release are angiotensin II, serum potassium and adrenocorticotropic hormone. However, other factors such as nitric oxide, endothelin and various pituitary and adipose-tissue factors can stimulate aldosterone synthesis. Once released, aldosterone mediates most of its effects through its binding to the mineralocorticoid receptor in the cytosol, which causes it to translocate to the nucleus, promoting changes in gene expression ("genomic" pathway). Aldosterone also activates specific molecular pathways within minutes through "non-genomic" ways, which could be either dependent or independent of mineralocorticoid receptor activation [4].

MR expression has been detected in classical and non-classical tissues. The classic effect of aldosterone is exerted in the epithelium of the aldosterone-sensitive distal nephron (ASDN), where MR activation stimulates renal sodium reabsorption and potassium excretion binding to the MR and controls sodium reabsorption and potassium secretion. Besides the traditional role in ion and water transport, these functions of mineralocorticoid receptors have also been detected in other cell types, especially in cardiac and vascular tissues. MR expression has also been identified in non-classical tissues, such as podocytes, fibroblasts, cardiomyocytes, endothelial, vascular smooth muscle cells, adipocytes and macrophages. Although known to be pathophysiological, its activation in non-classical tissues is not always due to the action of aldosterone, as 11β-HSD2 is not always expressed. MR expression may be upregulated in some pathological conditions, such as diabetes, heavy proteinuria, vascular aging, and hypertension, thus amplifying MR signaling [2,5,6].

Aldosterone promotes hypertension through sodium retention. This sound-known action remains a potential mechanism for both cardiac and renal injury. However, some of the impairment attributable to aldosterone and the benefits observed with its suppression and antagonism are complex and partially beyond their blood pressure lowering effects.

A rapid nongenomic mechanism initiated by mineralocorticoid receptor activation involves PI-3 kinase, protein kinase B, and heat shock protein 90-mediated stimulation showed that aldosterone inhibits depolarization-induced vasoconstriction in renal afferent arterioles of NO generation [7].

Nonhemodynamic actions of aldosterone may also participate in its renal and cardiac fibrotic consequences. Although the distal tubules are usually considered the targets of aldosterone action in the kidney, transcripts for the mineralocorticoid receptor have been detected in glomeruli, albeit at lower levels than in the distal tubular epithelium, most probably mediating fibrogenesis and sclerosis. There are rather old reports in vitro that

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showed that aldosterone does stimulate type IV collagen synthesis by mesangial cells and that vascular smooth muscle cells contain mineralocorticoid receptors that respond to aldosterone. It seems that an increasing number of locally and systemically acting factors have been associated with progressive renal injury [8]. Plasminogen activator inhibitor-1 levels were enhanced by aldosterone in the kidney and circulation, promoting thrombosis and extracellular matrix accumulation. Besides, data indicate that the TGF-β message is associated with aldosterone, suggesting that increased production of the profibrotic cytokine TGF-β is likely to be at least partly attributable to a direct action of aldosterone on renal tissue and not late nonspecific response to hypertensive renal injury [9]. Both TGF-β and the renin-angiotensin-aldosterone system (RAAS) participate in progressive renal damage, although the effect may be complex and may depend on hemodynamic and more direct actions. On the other hand, aldosterone and TGF-β1 added together produced dramatic synergistic effects on PAI-1 production and subsequent ECM accumulation. Thus, the activation of the elevated aldosterone induced by the renin-angiotensin-aldosterone system may amplify renin-angiotensin-aldosterone system profibrotic actions [10]. Therefore, both hypertensive and more direct cellular actions of aldosterone, including scarring, may account for its contributions to glomerulosclerosis and interstitial fibrosis.

Beyond organ fibrosis, some reports showed that mineralocorticoid receptors play a significant point in oxidative stress and inflammation. Due to genomic and non-genomic effects, it is raised reactive oxygen species (ROS) production (expressly by the enzyme NADPH oxidase), inflammation, and fibrosis, promoting tissue remodeling, vascular stiffening, and endothelial dysfunction being engaged in hypertension and cardiac and kidney damage [11].

Both macrophages and T cells have expressed MR, functioning as an essential transcriptional cellular phenotype and function regulator. In pathological conditions, this is being initiated even with normal or low aldosterone levels [12,13].

It was also noted that MR expression is enhanced in adipose tissue of murine models of obesity and obese human subjects. Different studies using MR antagonists and adipocyte-specific MR transgenic mice have demonstrated a crucial role of MR in insulin signaling and inflammation [14].

Although Angiotensin II plays an essential role in increased aldosterone level, it was shown that plasma aldosterone levels tend to grow with the duration of an ACE treatment (aldosterone breakthrough), suggesting that treatment with an ACE inhibitor was not sufficient in suppressing aldosterone synthesis [15,16]. In addition to ACE inhibition, that aldosterone blockade has an additional benefit in preventing organ damage. Besides reported studies in the heart, Bianchi *et al.* [17], more than a decade ago, showed that treatment with spironolactone might reduce proteinuria in patients with CKD. The newer and novel approaches to counteract this aldosterone breakthrough while emphasizing these agents' antihypertensive, antiproteinuric, anti-inflammation, and antifibrotic effects would be perfect, and mineralocorticoid receptor antagonists look to fit in this hole quite well, especially in CKD and diabetic nephropathy [18]. However, on the other hand, it is essential to note that steroidal MRAs are not indicated for treating patients with CKD and T2D. Their use is frequently associated with hyperkalemia, antiandrogenic adverse effects such as gynecomastia (for the nonselective MRA spironolactone), and eplerenone is contraindicated in hypertensive patients with creatinine clearance <30 mL/min and diabetic patients T2 with albuminuria [19]. Strategies to diminish aldosterone activation make sense, and drugs that interfere with the binding of aldosterone to its receptor to affect CKD is a relatively novel concept. Recently, we have had promising clinical trials with a new nonsteroidal structure of MRA [20].

Mineralocorticoid Receptor Antagonist Tolerability Study-Diabetic Nephropathy (ARTS-DN) was the first multicenter, randomized, double-blind, placebo-controlled, parallel-group, phase 2b study which compared finerenone (at the initial dose of 1.25 mg daily titrated up to 20 mg) with placebo in patients with type 2 diabetes and urinary albumin to creatinine ratio (UACR) ≥30 mg/g already being treated with an ACEI or an ARB. A significant decrease in UACR was detected with all doses of finerenone compared with placebo at 90 days. However, it would be noted that long-term effects on CKD progression or antifibrotic and anti-inflammatory properties have not been evaluated due to the short duration of the study where hyperkalemia but was observed in 6.3% of patients who received the maximal dose of finerenone in CKD stage 3 patients [21]. The largest metanalysis on the field including 31 studies presented by Sarafidis *et al*. [22,23], showed that using an MRA (alone or on top of RAS blockade) is linked with a significant proportional decrease in urine albumin or protein excretion from baseline. All three of spironolactone, eplerenone, and finerenone appear to reduce albuminuria potently. According to the analysis, using an MRA is associated with a mean increase in serum potassium by 0.22 mEq/l, increased more significantly with spironolactone than eplerenone and finerenone. Promising data of phase III clinical trial (ESAX-DN study) has also demonstrated the safety and efficacy of esaxerenone in patients with type 2 diabetes and microalbuminuria. Recently, we have an available very enthusiastic data of the FIDELIO-DKD trial (randomized, double-blind, placebo-controlled, parallel-group, multicenter trial which enrolled patients with an eGFR of 25-75 ml/min/1.73m2 and a UACR of 30-5000 mg/g). It was reported that finerenone, delayed the progression of kidney disease and improved cardiovascular outcomes in patients with advanced kidney disease and type 2

diabetes [24,25]. Moreover, Finerenone, in addition to standard medical therapy in patients with less-severe CKD and type 2 diabetes, reduced the risk of the study's primary endpoint of kidney failure or death from renal causes and reduced the risk of CV mortality, MI, stroke, or heart failure hospitalization among a population of about 7,400 patients which are the top results of FIGARO-DKD study [26].

Based on recent evidence, it is logical to suspect that if safe, MR blockade may contribute additional benefit when added to monotherapy with a RAS blocker by attenuating aldosterone breakthrough and through inhibition of deleterious effects aldosterone, such as renal inflammation and fibrosis and significantly retarding kidney disease progression. Preclinical and clinical studies indicate that MRAs reduce morbidity and mortality by reducing renal and cardiovascular risk [27]. Novel nonsteroidal MRAs are very selective and specifically inhibit MR, causing minimal hyperkalemia. The recent clinical trials of finerenone and esaxerenone in patients with kidney disease indicated a potential therapeutic role of nonsteroidal MRAs in CKD patients, especially with the new perspectives offered from novel treatments for hyperkalemia.

Conflict of interest statement. None declared.

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Review

Refractory Cytomegalovirus Infection in Renal Transplant Recipients: Current Knowledge and Future Perspective

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Abstract

Introduction. Resistant cytomegalovirus (CMV) in kidney transplant recipients represents an emerging issue. Prolonged hospitalization, increased utilization of resources, limited treatment options, and high toxicity of available treatment make the resistant disease a significant burden for the patients and a challenge for the treating physician.
Methods. This is a narrative review of the epidemiology, diagnosis and treatment options regarding resistant cytomegalovirus.
Discussion. Significant research has identified the main resistance mechanisms to the guideline-recommended treatment of resistant disease and for salvage and novel treatment options. The high toxicity of high dose ganciclovir and foscarnet pose an independent risk of treatment failure and graft loss. Several antiviral drugs and cytomegalovirus-specific T cells are being evaluated for their role in treating resistant cytomegalovirus disease.
Conclusion. Resistant CMV infection should be promptly recognized in kidney transplant recipients. Novel therapeutic approaches seem promising.

Key words: CMV, resistant, treatment, foscarnet, ganciclovir, letermovir

Introduction

Cytomegalovirus (CMV) is considered the most important pathogen after kidney transplantation. CMV disease can affect any organ system, including lungs, intestines, liver, brain, retina and the transplanted graft. Disease surveillance and treatment increase the costs of post-transplant care and increase the number of diagnostic and therapeutic procedures, creating a higher burden on the patient. Successful prevention via prophylaxis or preemptive treatment has significantly reduced the disease burden among kidney transplant recipients (KTRs). Exposure to antivirals has contributed to the development of mutations leading to resistance to treatment, particularly ganciclovir. Ganciclovir resistance is associated with more extended hospitalization, higher morbidity, and mortality in solid organ transplants [1,2]. Another increasingly recognized subpopulation of patients is those unresponsive to ganciclovir but without identifiable genetic mutations, termed treatment refractory CMV [3]. Additionally, second-line treatment options come with significant side-effect profiles, which themselves pose a risk for acute graft rejection, systemic toxicity and worse outcomes. Rates of reported ganciclovir-resistant CMV and treatment-refractory CMV are increasing. The novel treatment is under extensive research and is mainly used as salvage treatment when other options fail. Herein, we review resistant CMV epidemiology, genetics, diagnosis and treatment options.

Material and methods

This article is written as a narrative review based on relevant articles containing the terms "resistant cytomegalovirus" or "refractory cytomegalovirus" and "kidney transplant" or "solid organ transplant". Most relevant articles in PubMed were screened and selected. Subthemes involved were treatment resistance, refractory CMV, resistance monitoring, treatment of resistant disease, ganciclovir resistance. Previous reviews and references were screened for additional studies involving the following subthemes: cytomegalovirus resistance genetics, diagnostic methods, novel treatment.

Epidemiology of resistant CMV

CMV in the general population infects up to 60-100% of people. Similar to other members of its family, Herpesviridae, after primary infection, establishes lifelong latency. After impairment of the host's immune response, CMV can cause invasive disease and other indirect immunological effects [4]. CMV disease occurrence

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in KTRs without prophylaxis is dependent on the CMV serological match between the host and the donor, use of antilymphocyte antibodies, use of mTOR inhibitors and the existence of other risk factors [5-7]. Without prevention, the majority KTRs develop CMV infection and up to two-thirds develop CMV disease [5,8,9]. CMV resistance to treatment, primarily to ganciclovir, is sporadic in patients not treated with ganciclovir or valganciclovir [10]. CMV resistance is promoted in CMV D+/R- cases, prolonged ganciclovir exposure, high viral load and severe immunosuppression. A recent large meta-analysis has estimated the genotypic CMV resistance among solid organ transplants (SOT) to be around 12% and indicated that resistance rates are growing [11]. Resistance among patients on ganciclovir prophylaxis occurs 5-10% of cases [12,13]. Resistance has been described in patients on valganciclovir prophylaxis as well as preemptive treatment [14]. Two studies have associated suboptimal valganciclovir dosing with the development of ganciclovir resistance in solid organ transplant recipients [3,15]. Foscarnet is used as a second-line agent for treating ganciclovir resistant CMV, and although genotypic resistance to foscarnet has been described, there are no reports of treatment failure due to phenotypic resistance. In cases of failed viremia clearance on foscarnet treatment, subtherapeutic dosing has been identified as the presumed cause [3]. A recently published case series investigating the use of letermovir after foscarnet as a step down treatment for ganR-CMV disease described two cases of possible development of letermovir resistance, successfully treated with the addition of valganciclovir to the step-down regimen [16].

Mutations leading to treatment resistance

The list of gene mutations conferring CMV resistance is constantly increasing. Genotypic analyses in vivo and in vitro have elucidated the significance of many genetic mutations. Mutations conferring resistance to the main drugs used in CMV treatment are mutations in the UL97 and UL54 genes. The two genes encode a critical protein kinase and DNA polymerase, respectively [17]. Ganciclovir requires intact UL97 kinase function to become active and exhibit antiviral properties; therefore, UL97 gene mutations lead to ganciclovir and valganciclovir resistance. The DNA polymerase encoded by the UL54 gene is needed for the function of three common antivirals, ganciclovir, foscarnet and cidofovir, and its mutation confers resistance to these drugs. Sohrabi *et al*. published a cross-sectional study involving 58 KTRs with CMV and performed sequencing and analysis of the UL97 and UL54 genes. Although mutation in the UL97 gene vastly outnumbers mutations in the UL54 gene, mutation in UL97 alone confers low-level resistance compared to simultaneous mutations in UL97 and UL54 [17,18]. Most high-level GCV resistance is observed in dual UL97 and UL57 mutations [19]. UL56, UL51, and UL89 gene complex can affect viral terminase function and confer varying degrees of letermovir resistance. Mutations in UL89 and UL51 have only been shown to affect letermovir sensitivity in vitro. These studies have shown a low genetic barrier for the development of letermovir resistance, with in vitro resistance occurring sooner than resistance to foscarnet [20]. Cases of breakthrough infection and disease with letermovir-resistant virus have been reported in a phase 2 letermovir-prophylaxis study in stem cell recipients and adult and pediatric hematopoietic cell transplant recipients receiving letermovir for primary or secondary prophylaxis [21,22]. During maribavir selection pressure, UL27 mutations have been identified to cause low-grade resistance to maribavir, but these have not yet been isolated in vivo [22-24]. Additionally, most specific UL97 mutations which lead to maribavir resistance do not lead to ganciclovir mutations and vice versa [22,25]. Only one specific UL97 mutation was described, which resulted in maribavir resistance after prolonged ganciclovir exposure [26].

Diagnosis

Resistant or refractory CMV should be suspected in patients who display stable or progressive CMV viral loads or with persistent clinical symptoms despite adequate antiviral treatment for two weeks [10]. Two methods are most commonly used for monitoring CMV disease: reverse-transcriptase polymerase chain reaction (RT-PCR) and antigenemia assays. RT-PCR is more expensive but superior, as it has a higher sensitivity and is particularly more reliable at lower viremia levels (<1000 DNA copies/mL) [5]. After a suspected resistant or refractory disease, genotypic analysis of the UL97 and UL54 genes must be performed, and further management is guided based on these results. In situations where genotype analysis is unavailable, treatment should be changed empirically [10]. An important note is that rising viral loads within the first two weeks of treatment are not predictors of resistance development, and resistance studies are not recommended in these cases [27]. The sample of choice for genotypic studies is plasma, as there were reports of inconsistent findings between analyses of cerebrospinal fluid, leukocytes, bronchoalveolar lavage, and tissue samples [10,28]. Several limitations regarding the use of genotypic tests exist. There is a lack of standardization of genotypic assays. They may not target all the genetic loci of interest and may report mutations that have not been definitely linked to confer phenotypic resistance. To detect resistance, the strain must represent a certain proportion of the total viral population to be detectable [29].

Treatment of resistant disease

After the establishment of the diagnosis of ganciclovir resistant CMV, several established treatment options exist. There are reports of off-label use of leflunomide, artesunate, letermovir, and other antivirals as salvage therapy for more refractory cases. Additionally, adoptive immunotherapy has been reported as a successful treatment in several cases. Due to the severe and limiting side-effect profile of these drugs, factors that need to be considered when choosing the appropriate agent include the results of genotypic analyses, presence of neutropenia, degree of renal function, or renal failure, immunosuppressive regimen, and comorbidities present.

Ganciclovir

Ganciclovir is a 20-deoxyguanosine analog, and serves as a competitive substrate for a CMV DNA polymerase encoded by the UL54 gene. To act as a substrate for the polymerase, it requires phosphorylation mediated by the UL97 protein kinase, transforming it to ganciclovir-monophosphate. The subsequent bi- and tri-phosphorylation by host kinases results in the active form ganciclovir triphosphate. It acts by incorporation into the DNA chain, thereby terminating the synthesis of CMV DNA [20,30]. High or intermediate-dose ganciclovir (up to 10mg/kg/12h if normal renal function) can be used in patients with the non-severe disease and in whom the use of foscarnet is not recommended [10]. There is increasing evidence that even when high-grade resistance mutations are confirmed, treatment by increasing the ganciclovir dose is sufficient for viral replication control [31].
Interestingly, the IMPACT trial studied six asymptomatic or low-level disease patients with resistant CMV strains and demonstrated viral load clearance in half of the patients without antiviral therapy [31,32]. Despite these findings, treatment of documented CMV viremia is recommended to prevent the indirect effects of the virus. There are proposed benefits of allowing viremia for the development of virus-specific immunity. However, the significance of this immunity, particularly in patients with proven resistant CMV, is uncertain [10]. It must be noted that all patients in the study had very low viral loads and the cases were non-severe. Considering the myelosuppressive effects of high dose ganciclovir, caution is advised in using high dose ganciclovir for CMV with high-level resistance mutations [33].

Foscarnet

Foscarnet is a guideline-recommended agent for proven ganciclovir resistant CMV disease and as first-line empiric therapy for suspected ganciclovir resistant CMV in situations when genotypic studies are not available [10,20,34,35]. Foscarnet is a pyrophosphate analog that inhibits a CMV DNA polymerase encoded by the UL54 gene, resulting in the termination of CMV DNA synthesis [20]. Unlike ganciclovir, it does not require phosphorylation for its antiviral activity and is therefore not affected by UL97 mutations. Limiting its use are its side effects, notably nephrotoxicity, electrolyte disturbances and genitourinary infections. As with many antivirals, nephrotoxicity can occur via calcium crystal deposition. Specific for foscarnet is crystal deposition in the glomerular capillaries rather than in the tubules [36]. Kidney functional and pathological changes are reversible if the fibrotic changes are not severe and the patient receives adequate hydration [36,37]. Notably, treatment failure due to foscarnet toxicity is not uncommon in KTRs, as they are receiving other nephrotoxic drugs, including calcineurin inhibitors, and are at risk for other electrolyte imbalances [14,33].

Combination treatment with foscarnet and ganciclovir

Indications of a synergistic effect when using foscarnet and ganciclovir simultaneously exist [33,38]. The mechanism of synergy is not elucidated. However, the combined nephrotoxicity and effects on the bone marrow decrease the utility of this approach. No data regarding the use of this protocol exclusively in KTRs exist, and no studies directly compared foscarnet or high dose ganciclovir alone versus a combination of the two.

Letermovir

Letermovir targets the CMV terminase complex and inhibits the cleavage of CMV DNA and its package into capsids [39]. Considering its different mechanism of action, mutations in UL54 and UL97 do not affect letermovir susceptibility, and there is no cross-resistance with ganciclovir, foscarnet, maribavir, or cidofovir [40]. Primarily used and investigated in hematologic stem cell transplant recipients, it is approved as primary CMV prophylaxis in HSCT recipients. Combination treatment of letermovir with ganciclovir or cidofovir has resulted in additive effects and an additive/minor antagonistic effect when used concurrently with foscarnet against CMV in cell cultures [39]. As mentioned earlier, the genetic barrier to letermovir resistance development is low, and monitoring for resistance may be necessary. In a study of resistant CMV retinitis where letermovir was used as salvage treatment, three of four patients failed to clear CMV viral loads, and two developed genotypically confirmed resistance. Of note, letermovir was used after treatment with ganciclovir, valganciclovir, foscarnet and CMV immunoglobulins [41]. Letermovir has significant drug interactions with cyclosporine, and half dosing of letermovir is necessary when co-administered with cyclosporine [42]. Advantages of letermovir include its good oral availability and good patient tolerance. Currently, it is only used as off-label salvage therapy for treatment-resistant CMV. Further studies will elucidate its potential in

concurrent treatment with other novel drugs, including artesunate, which may have synergistic effects [43].

Cidofovir

Cidofovir is an acyclic monophosphate deoxycytidine analog that causes premature termination of CMV DNA synthesis. It acts as a nuclear analog substrate for the UL54 polymerase, and the reduced sensibility to cidofovir has been mapped to UL54 [20]. Mono-resistance to cidofovir is rare, and it frequently appears with cross-resistance to ganciclovir. It is currently used as an alternative agent for resistant CMV in solid organ transplant recipients, and its use is limited by high nephrotoxicity [40].

Brincidofovir

Brincidofovir is an oral lipid conjugate formulation of cidofovir, mainly investigated as CMV prophylaxis in HSCT recipients. Its lipid formulation enabled lower renal toxicity and increased in vitro toxicity compared to cidofovir [44]. A phase 3 study of brincidofovir prophylaxis in CMV HSCT recipients failed to meet its primary endpoints, and currently, oral brincidofovir is not developed as a treatment for CMV [22,40,45].

Leflunomide

Leflunomide is an isoxazole-derivative drug primarily used to treat rheumatoid arthritis and prevent and treat solid organ rejection [46]. It has shown antiviral activity against CMV, BK virus, and herpes simplex virus. Leflunomide does not share the mechanism of action of other antivirals, including ganciclovir, foscarnet and cidofovir, making cross-resistance an unlikely occurrence [47]. Hepatotoxicity, bone marrow suppression and its long half-life represent disadvantages of leflunomide [29,46]. Definitive evidence of clinical benefit in the treatment of resistant CMV is lacking. However, case reports and case series of its use have been published [29,46,48,49].

Maribavir

Maribavir is an inhibitor of the viral pUL97 kinase activity and interferes with nascent viral particles' morphogenesis and nuclear egress [39]. Maribavir does not require phosphorylation for conversion to an active form, rendering it particularly useful in UL54 mutations [40]. Maribavir has a favorable safety profile, good oral bioavailability and lower toxicity than currently approved drugs [50]. Tacrolimus and sirolimus levels increased in 10% of patients treated with maribavir, and dose adjustments are recommended [39,51]. Maribavir cannot be administered concomitantly with ganciclovir. A recent study evaluating the appropriate maribavir dose for refractory or resistant CMV reported discontinuation of the drug due to adverse effects (including CMV infection or disease) in 34% of the involved patients. The most common reported adverse effects are dysgeusia, nausea, and vomiting. Neutropenia is dose-independent. Treatment success was reported in two-thirds of treated patients [52].

Artesunate

Artesunate is an artemisinin derivative used primarily as an antimalarial agent. It has been shown to decrease CMV DNA replication by a pathway independent of commonly used antivirals. Studies demonstrated a synergistic effect combined with ganciclovir and additive effects with foscarnet and cidofovir [33]. Case reports of its use against resistant CMV show mixed outcomes [29]. In the treatment of malaria, artesunate has been shown to be well tolerated [33].

Filociclovir (Cyclopravir)

Filociclovir is a guanosine analog and acts by terminating DNA synthesis. Similar to ganciclovir, it requires phosphorylation by UL97 kinase [33]. In vitro studies have shown that it is five times more potent than ganciclovir against CMV, which may result from it being a better substrate for UL97 than ganciclovir [22]. Filociclovir shows activity against HHV-6. Currently, no available data of its use against CMV in humans exist. Clinical trials are underway [33].

Adoptive T cell therapy

Adoptive immunotherapy involves using HLA matched transfused donor T cells (CD4+ and CD8+) to restore adequate immunity without the occurrence of side effects associated with antivirals. The primary experiences draw from hematologic stem cell transplant recipients, in whom this therapy was used as an adjunct to preemptive antiviral therapy and the treatment of refractory CMV infections [22]. The main presumed benefit of this approach for KTRs is the presumed allograft stability. In SOTs, this approach was less explored, presumably due to the lack of HLA-matched donors and due to the T cell response atenuation by the immunosuppressive treatment used. However, this became a more explored field after successfully treated severe CMV disease in a KTR using third-party CMV-specific T cells [53]. The creation of third-party cell banks and cell registries could help create readily available treatment [54].

Currently, several clinical trials involving both HCTs and SOTs are evaluating the use of T-cell transfusions for treatment of CMV infection or severe CMV disease (NCT03266640, NCT04364178, NCT03665675). Furthermore, protocols for the in vitro selection and expansion of CMV-specific T-cells have been developed [29]. A

recent report from a prospective study reported treatment of recurrent or resistant CMV disease in 13 SOT recipients with autologous T-cell transfusions involving 4 KTRs. Improvement in symptoms was reported in 11/13 enrolled patients, including reduction of viremia and/or reduction or cessation of antivirals [55]. None of the patients who received adoptive CMV-specific T-cell therapy showed moderate or severe treatment-related adverse effects.

CMV intravenous immune globulin

The role of intravenous immunoglobulins (IVIG) in the treatment of CMV disease is unclear, and there are conflicting reports. The treatment is well tolerated and is currently mainly used as an adjunct treatment for resistant or refractory disease [40]. Benefits for CMV pneumonia are poorly defined, and extensive studies fail to show treatment effects [22]. However, a German team recently published a case report of a successfully treated KTR with multi-drug resistant CMV by immunosuppression change and high dose CMV specific IVIG. It is postulated that the combined effects of mTOR inhibitors and induction of specific CMV immunity contributed to viral control in their patient [56]. In addition, the opsonizing activity of immunoglobulins may favor uptake of CMV antigens into antigen-presenting cells and thereby increase antigen-presentation and their stimulatory capacity toward CMV-specific T cells.

Conclusion

Resistant CMV infection remains a major challenge after kidney transplantation. It should be promptly recognized in kidney transplant recipients. Novel therapeutic approaches seem promising.

Conflict of interest statement. None declared.

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Review

The Impact of Physical Therapy on Patients with and post COVID-19

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Abstract

Novel coronavirus, also known as SARS-CoV-2, was first discovered at the end of the year 2019. Since then, it has affected 124 million people and caused the death of 2.73 million people around the world. This viral infection damages the lungs, making it difficult to breathe. Along with medical management, physical therapy has shown immense improvement in patients suffering from COVID-19. Respiratory therapy and manual mobilization therapy provided under the established guidelines have proven to be effective to increase lung capacity, treat dyspnea and prevent muscular weakness in hospitalized patients. More research is required to establish further guidelines.

Keywords: physical therapy, COVID-19, rehabilitation, Chest physiotherapy

Introduction

Coronaviruses (CoV) are known as the largest RNA viruses. They range from 65 to 125 nm in diameter. The nucleic acid genome of coronavirus is a single-stranded RNA and ranges between 26 to 32 kb in length [1]. Six various forms of coronavirus that caused diseases in humans have been found since 1960. This newly discovered SARS-CoV-2 is the seventh one [2]. While the previous cases of Coronavirus were less infectious and were mainly associated with mild symptoms, SARS-CoV-2 causes much more severe consequences that might potentially lead to fatal scenarios [3]. Globally, the infection that is caused by SARS-CoV-2 is known as Coronavirus Disease 2019 (COVID-19).

The world is struggling against this deadly virus and the management is predominantly supportive and symptomatic amidst the absence of validated antiviral drugs. Fever and cough are the primary symptoms of COVID-19 case [4]. Some patients with respiratory distress also require supplementary oxygen supply due to the decreased oxygen saturation [5]. Along with the medical treatment, pulmonary rehabilitation is also important when COVID-19 positive patients. Pulmonary rehabilitation is defined by the American Thoracic Society/European Respiratory Society as a comprehensive intervention regime that involves patient assessment, followed by the tailored therapies for patients including exercise training and education to improve the physical and respiratory health of patients with respiratory disease [6]. In case of COVID-19 patients, pulmonary rehabilitation aims to alleviate symptoms of dyspnea and anxiety, reduces complications, limits disability, and improves the overall quality of life [7]. Therefore, physiotherapy plays a crucial role in the treatment of patients, whether it is during critical care, inpatient departments, follow-ups or at home [8]. Here are a few treatment approaches used by the physical therapists i.e., Deep breathing exercises, Mechanical airway clearance, Bronchial hygiene techniques, Active movement of extremities (both upper and upper), chest oscillations, Flutter device and Cornet devices along with Non invasive ventilation, High flow nasal cannula, and conventional O2 Therapy. These maneuvers help loosen up the mucus, reduce the load from mechanical ventilation and improve breathing. Despite the important role and the impact of physical therapy when treating critical patients, its importance remains overlooked. Little literature is available on the guidelines regarding implementation of physiotherapy practices and its impact on the patient's health. The objective of this review article is to extract information from the already available literature and assemble it all to find the impact of physical therapy on patients who are currently affected by COVID-19, as well as to see its impact on the patients that have already recovered from COVID-19. In conclusion, the fundamental rationale of writing this review article is to make a readable synthesis of the best literature sources on an important research topic. All the data available in different studies will be assembled in one single literature review.

Material and methods

The present review was conducted and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses (Figure 1). The figure clearly states 4 phases which are: Included, Eligibility, Screening and Identification on how the study was carried out.

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Firstly, records identified through database searching (n=50) along with additional records identified through other sources (n=10). Next, after carefully removing the duplicates (n=40), the screening starts (n=30) along with exclusion (n=10). As moving along to eligibility phase which is fairly important, we are left with the studies that are included in qualitative synthesis (n=8).

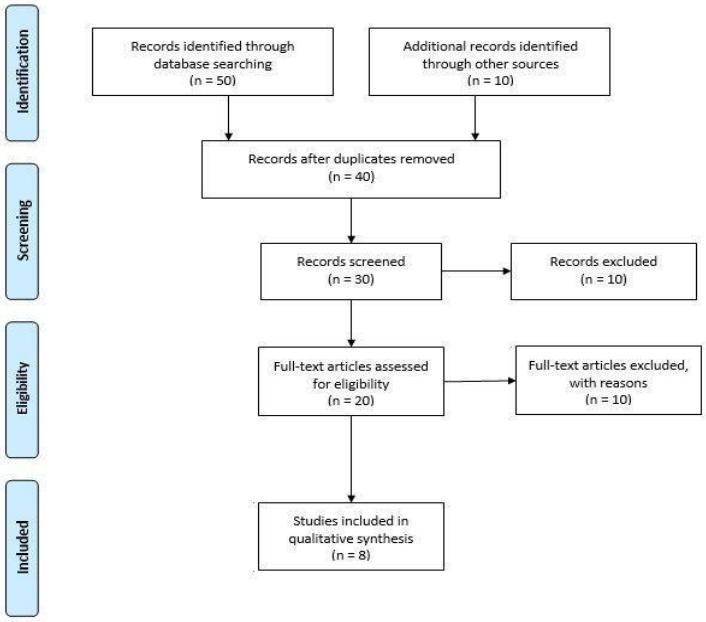

Fig. 1. Search strategy for the review

Search strategy

Several articles from PubMed, Medline, Pedro, Central, Scopus and Google scholar databases were reviewed from 2019-2021. The following keywords: Physical Therapy, COVID-19, Coronavirus, respiratory therapy was used in combination or individually by using Boolean operations "OR" and "AND". Only completed studies published in English focused on Physical Therapy as a treatment intervention for patients currently suffering from COVID-19 or those who recovered from COVID-19 were included in this review. Firstly, the titles and abstracts were screened for relevant studies, and duplicates were excluded. Secondly, the full texts were downloaded and assessed for eligibility. The reference list of included publications was hand searched for additional relevant studies. This process was carried out independently by Xhorxhina Peshku. Any difference was resolved by consensus.

Study selection

Inclusion criteria:
The inclusion criteria for the studies were as follow:

1. The studies were either randomized controlled trials (RCTs), cluster randomized controlled trials (CRCTs), or controlled clinical trials (CCTs), where the physical therapy group was compared to any control group.
2. The studies that evaluated physical therapy intervention for COVID-19 (any training duration and treatment setting, with and without adjunct treatment).
3. The studies that were conducted on human participants affected from COVID-19.
4. Participants with age greater than 18.
5. The studies that were published in peer-reviewed academic journals or conference proceedings.

Exclusion criteria:

1. The studies published in any language other than English.
2. Studies for which the full text was not found.
3. Technical papers.
4. Clinical trials not completed yet.

Study quality assessment

The included studies were assessed using Robins-1 tool 11 (McGuinness & Higgins, 2020).

Data collection

Year of publication and author's name, type and place of intervention, description of intervention, outcomes and result of the study were extracted.

Results

Following eight studies, the results of these studies

Table 1. Summary of Review articles

Author's name	Study type	Description of intervention	Place of intervention	Outcome
Arora, Jain, & Khare, 2020 (10)	Systematic Review	Mucus removal technique (endotracheal suctioning and manual thorax percussions) Chest physiotherapy (percussion, vibration, postural drainage for bedridden, active breathing exercises)	In patient department	Reduces potential pulmonary and systematic complication Low chance of developing Hospital infection
Battaglini *et al*., 2020 (11)	Review Article	Chest physiotherapy Prone positioning Active cycle of breathing exercises Neuromuscular drainage	In patient department	Improved long term respiratory function
Kalirathinam, Guruchandran, & Subramani, 2020 (12)	Review article	Neuromuscular electrical stimulation Postural drainage Mobilization Bronchial clearance technique	In patient department	Improving mucus drainage Respiratory muscle strengthening Preventing disability
Kachpile, Lohakare, Jiandani, & Salagre, 2020 (13)	Case report	Prone position for 15 minutes to 30 minutes, 3-4 times/day. Posterobasal segmental breathing exercises proprioceptive neuromuscular facilitation Body mobility exercise	In patient department	Lung expansion mproved chest mobility 99% oxygen saturation upon discharge from hospital
Liu *et al*., 2020 (14)	Randomized control trial	2 sessions/ week for Six-week of respiratory therapy	Inpatient and outpatient	Improved respiratory function. Respiratory muscle training
da Silva e Silva *et al*., 2020 (15)	Original Article	Secretion removal technique, directed cough and chest oscillations, Mobilization 2-3 times a day for first three days. 3-5 minutes progressing according to tolerability	In patient department	Treating functional limitations Improves aerobic physical performance
Vitacca *et al*., 2020 (16)	Positional paper	Chest Physiotherapy Limb mobility exercises	Inpatient department	Reduction of dyspnea Training of skeletal muscles
T. J. Wang *et al*., 2020 (7)	Analysis	Airway clearance technique (lung volume recruitment, positioning, forced expiratory maneuver) Mobilization	In patient and home rehabilitation	Improve symptoms of dyspnea, Minimizing disability

have been reviewed. A summary regarding the intervention used, and the impact of the physical therapy intervention on the improvement of COVID-19 patients' health is mentioned in table 1.

One of the eight studies was a randomized controlled trial, one was a systematic review article, two of the studies were review articles, one was a case report, one was original article, positional paper and analysis report. Positive outcome was recorded from all the studies regarding use of physical therapy for respiratory management in patients with COVID-19.

Discussion

Not all of the reviewed articles have directly assessed or monitored the impact of physical therapy on COVID-19 patients, but the information regarding the effectiveness of rehabilitation is being extracted from them. Currently, very limited evidence exists showing that chest physiotherapy should be administered and proved effective in the acute phase of the disease in patients with hypoxemic respiratory failure. However, patients with productive cough may benefit from maneuvers that could stimulate coughing [17]. Patients who are suffering from COVID-19 and are facing deteriorating physical conditions, such as reduced exercise capacity, dyspnea, fatigue and myalgia might also benefit from the respiratory physiotherapy 17 (Huang *et al*., 2020). This is due to the fact that prolonged hospitalization and decreased activity level reduce muscle strength and cardiorespiratory capacity [18]. Therefore, patients should be encouraged to perform functional and breathing exercises while monitoring their vitals. Those patients who cannot carry an active lifestyle, must be aided. Classically critical patients show reduction in duration of mechanical ventilation and hospital readmissions who underwent early mobilization [19]. Therefore, early mobilization should be encouraged in COVID-19 patients. The reviewed studies have shown that different techniques of respiratory therapy such as airway clearance, postural drainage, manual thorax percussion and active cycle of breathing techniques have proved to reduce the following symptoms of COVID-19: dyspnea and anxiety. They also improved the oxygen saturation, respiratory function and respiratory muscular strength.

However, there is still not enough sufficient evidence available in this domain that could monitor the long-term effects of respiratory physiotherapy in patients

suffering from COVID-19 and their post COVID-19 lung capacity. More work should be done in order to record its effectiveness and to establish better guidelines for further intervention.

Conclusion

As the whole world is going through the pandemic, medical professionals and researchers are still struggling to come up with effective treatment options for patients suffering from novel coronavirus.
As this virus mostly affects the lungs of patients, more emphasis is being put on improving respiratory health. Physical therapy has shown to achieve improvement in breathing rate, lung compliance, respiratory muscle strengthening and overall functional capacity of patients. However more research is needed.

Conflict of interest statement. None declared.

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Original article

Analgesia in Kidney Transplant Recipients

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Abstract

Introduction. To our knowledge, currently no consensus or guidelines exist regarding perioperative and postoperative analgesia management in renal transplant recipients.
Methods. We conducted an observational prospective clinical study to evaluate the analgesia management practice in kudney transplant recipients. All consecutive patients who underwent kidney transplant surgery were enrolled in this observational clinical study. According to current analgesia management practice in our institution, patients were divided in two groups: patients who received general anesthesia and epidural analgesia were group E, and patients who received general anesthesia and i.v. analgesia were group G. The primary outcome measure in this study was VAS score and 24 h analgesia requirements. The second outcome measures were complications and/or side effects related to analgesia treatment.
Results. Group E had lower VAS pain score both at rest and on movement but only in the first 2 h, (VAS at rest E. 3.1±0.3 vs. G. 4.0±0.3, VAS on movement E. 4.2±0.6 vs. G. 4.5±0.3, $p<0.05$). The pain score by VAS scale did not differ between the groups at 6 h, 12 h and 24 h postoperatively, p=NS. Additionally, a small difference was noticed in side effects. Patients in group E had reported more side effects than patients in group G.
Conclusion. The study highlighted the variety in clinical practice regarding anesthesiologist preferences for pain management in kidney transplant recipients. This evaluation did not show any difference between anesthetic techniques and clinical results.

Keywords: kidney transplant, analgesia, epidural, analgesia management

Introduction

In our country since 1977 kidney transplant has been the preferred treatment of patients with end-stage kidney disease [1,2]. For optimizing surgical outcome adequate analgesia treatment in renal transplant recipients requires satisfactory pain relief, maintenance of physiological homeostasis and minimal nephrotoxicity [1,3,4]. To our knowledge, currently no consensus or guidelines exist regarding perioperative and postoperative analgesia management in renal transplant [5]. A significant number of clinical research is investigating the analgesia management, but the majority of these studies exclude renal transplant recipients [6], resulting in a limited evidence-based analgesia management in this complex patient cohort [5]. Many different strategies and techniques have been reported in the literature [1,3]. These patients usually are managed with a combined general and regional anesthesia. Many anesthesiologists avoid regional anesthesia due to concerns regarding coagulation disorders in kidney disease patients. As well as use of anticoagulant drugs before surgery due to comorbidities and use of anticoagulants intraoperative and postoperative for improving graft survival [7].

Material and methods

In our hospital, there is heterogeneity in management of analgesia in renal transplant recipients. Therefore, to provide an evidence-based management, we conducted an observational clinical study in order to encompass the entire perioperative and postoperative period and to generate an overview of current practice and to evaluate the efficacy of different analgesia regimens.
Hospital Ethics Committee approval and patient written informed consent were obtained before the beginning of the study. Every patient who underwent open surgery for kidney transplant during the period of

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January 2019 until August 2020was enrolled in the study. Excluded from the study were patients with any psychiatric disorder. The American Society of Anesthesiologist (ASA) score was assessed in all patients. The observers providing postoperative evaluation of patients were unaware of the type of anesthesia and analgesia method. According to current analgesia management practice in our institution, patients were divided in two groups: Group E (patients who received a combined general anesthesia and epidural analgesia) and Group G (patients who received only general anesthesia and i.v. analgesia). All patients did not eat or drink after midnight the night before surgery and premedication with Diazepam 5 mg orally was administered 2 h before surgery. A standard hemodynamic monitoring [electrocardiogram, pulse-oximetry, non-invasive blood pressure] was made before induction in anesthesia. According to patient's medical history, physical examination, medical analysis and anesthesiologist preferences, the analgesia technique was determined. Epidural catheter was placed in Group E, before induction in anesthesia. Patients who received epidural were in a sitting position L1-L2, epidural space was identified and with Touhy 18G needle and loss of resistance technique epidural catheter was placed. Afterwards negativity was confirmed with bupivacaine 0.5%-2 ml and as loading dose fentanyl 0.1 mcg was used. All patients were induced in anesthesia according to institutional protocol with midazolam 1 or 2 mg, fentanyl 2-10 mcg/kg, propofol 1-2 mg/kg and atracurium 0.5 mg/kg. Volume guarantied/pressure controlled mechanical ventilation (Datex-Ohmeda Avance S-5) with PEEP 5-7 cmH_2O and mixture of 50% oxygen/air was placed. Respiratory rate and tidal volume from 6-8 ml/kg were adjusted according to end-expiratory CO_2 (Et CO_2) and arterial blood gas analyses. Intra-arterial line and central venous line with continuous invasive pressure measurements were placed. Anesthesia was maintained with total intravenous anesthesia (remifentanil 0.25-0.5 mcg/kg/min and propofol 0.5-1 mg/kg). Except received fentanyl as loading dose in the epidural catheter in E group, nothing else was used until the end of surgery, when patients were transferred to transplantation unit and the time for the first analgesia requirement was noted. At the time of analgesia requirement, in group E continuous infusion with bupivacaine 0.125% and morphine 0.1 mg/ml was given starting with 2 ml/h. In group G after remifentanyl infusion was discontinued in the end of surgery if there was need of rescue analgesia fentanyl was used in 0,001 mcg/kg and patients were transferred to transplantation unit. The time for the first analgesia requirement was noted and the anesthesiologist and nephrologist in charge prescribed analgesics drugs.

We observed and analyzed the following parameters: patient demographic data, analgesia management in terms of time, dose, technique, anesthesia time and surgical time. Patients graded their pain on a visual linear analog scale (Visual Analogue Scale-VAS) of 1-10. VAS was noted at rest and during mobilization at 2 h, 6 h, 12 h, and 24 h postoperatively. Time for the first rescue analgesic was noted and total analgesic drugs received during 24 h. Any complication and side effects related to analgesia treatment were noted as well.

The primary outcome measure in this study was VAS score and 24 h analgesia requirements. The second outcome measures were complications and/or side effects related to analgesia treatment.

Statistical analysis was performed with the statistical package of social science, SPSS program. Categorical variables were expressed as number (percentage) and continuous variables as mean ± standard deviation. P values <0.05 were considered to be statistically significant.

Results

During the study period, 24 patients were enrolled in the study. One patient was excluded from the analysis due to acute kidney rejection and one patient had accidental catheter removal. He was also excluded from the analysis. Out of 22 patients, group E (where combined epidural analgesia and general anesthesia was used) included 11 patients (50%), and group G (where general anesthesia and i.v. analgesia was used) also included 11 patients (50%) (Figure 1). None of group E patients received any other kind of regional anesthesia except epidural. Three patients in G group had required rescue analgesia in the end of the surgery. There was no significant difference in demographic profile and clinical data of patients between both groups. Only two patients from group E and one patient from group G did not undergo regular scheduled dialysis (Table 1).

Table 1. Demographic and clinical profile

Demographic and clinical data	Group E [n=11]	Group G [n=11]
Age [years] mean±SD	40.54±16.5	37.63±15.22
Female/Male	3/8	2/9
ASA II/III	2/9	1/9
Duration of surgery [minutes] mean±SD	201±26	203±31

*ASA- American society of Anesthesiologists; n = number of patients; SD-Standard deviation

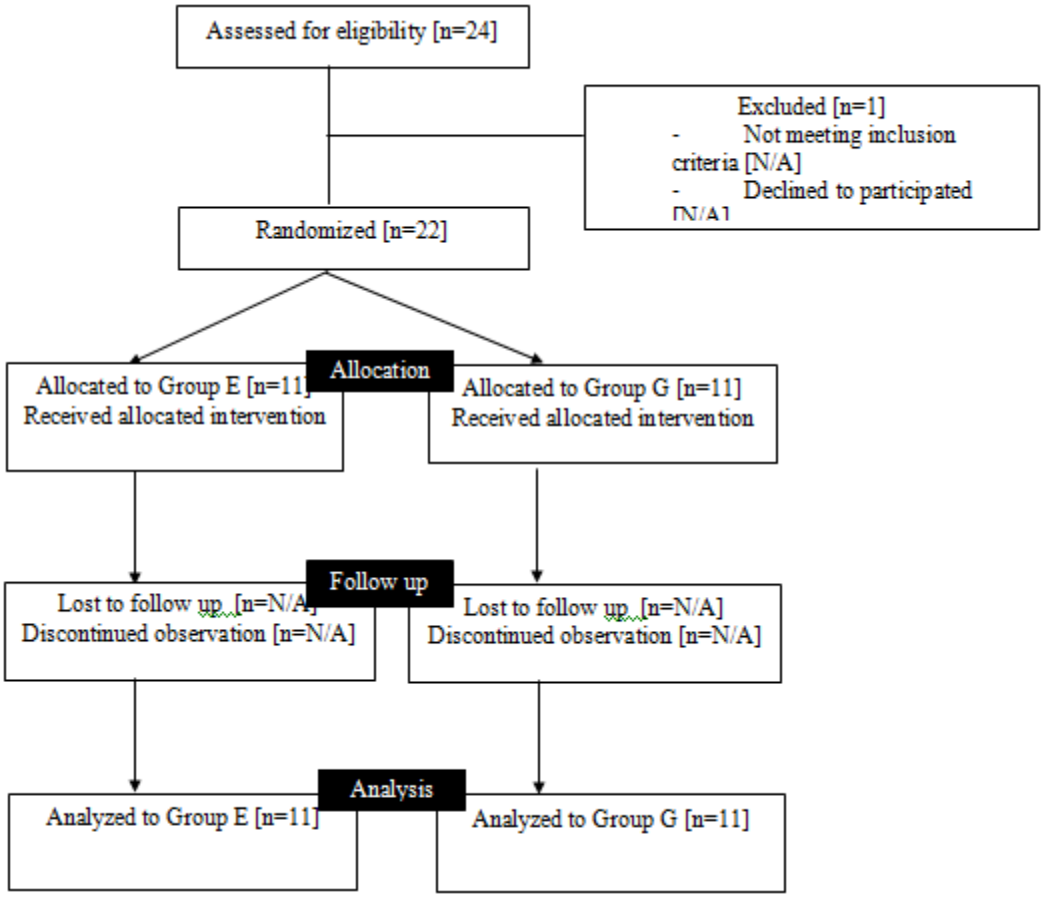

Fig. 1. Consolidated standards of reporting trials flow diagram

Table 2. Postoperative analgesic requirements in first 24h

Analgesia management	Group E (n=11)	Group G (n=11)
TFAR (minutes) mean±SD	35±24.15	15±12.12
EPDK total continuous infusion (h)	14±8.9	/
Nº of patients received opioid analgesics	/	4
Nº of patients received NSAID	1	/
Nº of patients received Paracetamol	1	11

*TFAR – Time to first analgesia requirements; n = number of patients; EPDK – epidural catheter; NSAID – non-steroidal anti-inflammatory drug

Group E had lower VAS pain score both at rest and on movement but only in the first 2 h (VAS at rest E. 3.1±0.3 vs. G. 4.0±0.3, VAS on movement E. 4.2±0.6 vs. G. 4.5±0.3) ($p<0.05$). The pain score by VAS scale did not differ between groups at 6 h, 12 h and 24 h postoperatively (p=NS) (Table 2, Table 3, Table 4, Figure 2, Figure 3).

Table 3. Visual analog scores (VAS) on rest

Time (h)	Group E (n=11)	Group G (n=11)	P value
2h	3.1 ± 0.3	4.0 ± 0.3	P < 0.005
6h	2.7 ± 0.4	2.9 ± 0.5	P = NS
12h	2.1 ± 0.6	2.0 ± 0.6	P = NS
24h	1.9 ± 0.1	1.9 ± 0.4	P = NS

*n = number of patients; p = significance between the groups; NS = non-significant

Table 4. Visual analog scores (VAS) on movement

Time (h)	Group E (n=11)	Group G (n=11)	P value
2h	4.2±0.6	5.1±0.3	P < 0.005
6h	3.1±0.1	3.0±0.3	P = NS
12h	2.9±0.5	3.1±0.6	P = NS
24h	2.4±0.2	2.6±0.4	P = NS

*n = number of patients; p = significance between the groups; NS = non-significant

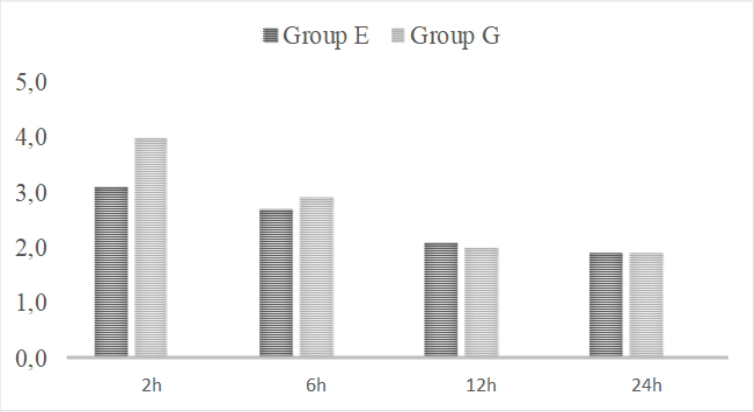

Fig. 2. Graph depicting VAS at rest

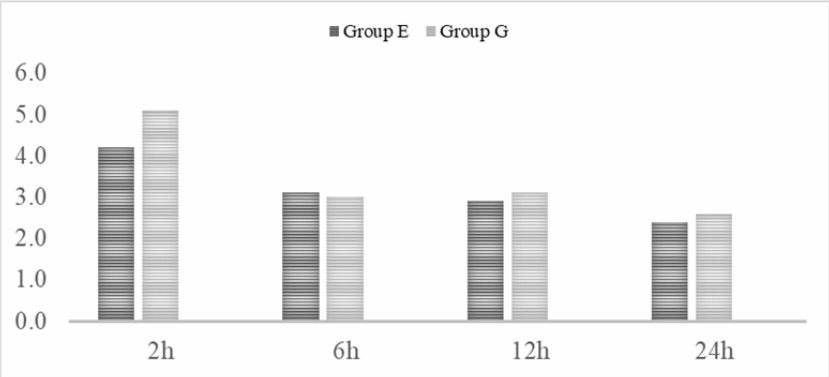

Fig. 3. Graph depicting VAS at movement

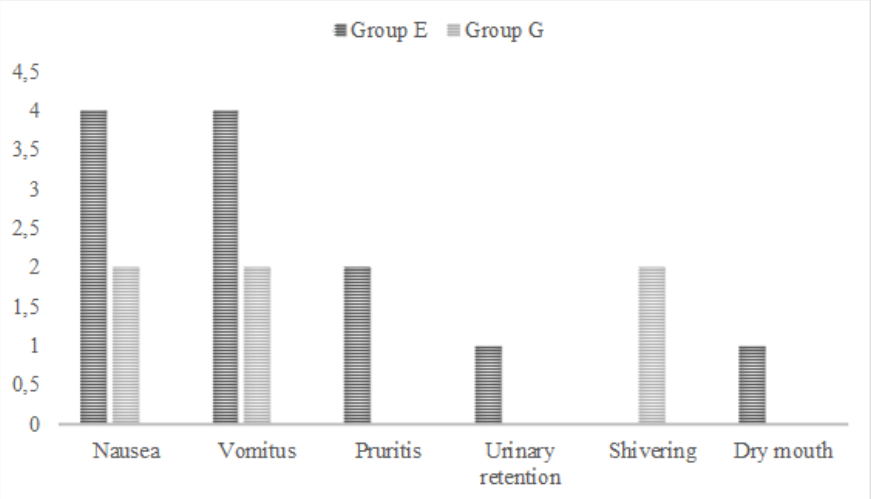

Fig. 4. Incidence of side effects in the Groups E and G

The evaluation of complications and side effects showed the highest incidence in E group. Except from accidental catheter removal in one patient, who was excluded from the analysis, there was catheter blockage in another patient. Due to hemorrhage in the surrounding tissue, the epidural catheter was preliminary removed on the second postoperative day after evaluation was finished. However, the patient had no need of it anymore. Nausea, vomiting and pruritus were reported most often. Even 4 patients felt nausea and vomiting, and 2 patients complained of pruritus. One patient complained of urinary retention and one of dry mouth. No other complication or side effects such as respiratory depression was noticed. On the other hand, in-group G, two out of four patients who received rescue analgesia with opioids had nausea and vomiting. Two patients reported shivering and there was no report of any other complication or side effects in group G (Figure 4).

Discussion

It is difficult to quantify/assess the contribution of good analgesia in good outcome of kidney transplant recipients. Not satisfactory analgesia, fear of possible graft rejection, anxiety and stress increase the risk of a significant postoperative pain in kidney transplant recipients. However, the management of analgesia should not compromise the graft function [8-10]. The results of our study indicated that epidural analgesia and i.v. analgesic drugs are used commonly among anesthesiologists in our institution. On the other hand, other regional anesthesia techniques are not a preferred choice and none of our patients received other kind of regional technique except epidural. On the contrary, there are many reports in the literature regarding the use of regional analgesia techniques for kidney transplant recipients. The most often used is transversus abdominis plain block. Currently no superior recommendation of transversus abdominis plain block over a combined general and epidural or general anesthesia exists [7, 11,12]. In our evaluation, only one patient received NSAID. Knowing the toxicity of NSAIDS there should be always a suspicion in their use, especially if edema, hypertension, decreased GFR or increased metabolism degradation products (creatinine and urea) exist [13]. The choice for analgesia management depends on the characteristics including hemodynamically stability, minimal blood loss intraoperative, early mobilization, satisfactory analgesia, and lower incidence of side effects and complications [14]. The side effects in both groups were different. In group E a larger number of patients suffered from side effects and had complications (72%) compared to group G (18%), where two patients who were shivering, received an additional opioid analgesic (tramadol) and despite the use of ondansetron had nausea and vomiting. Similar results were presented in the randomized study of Bajwa *et al*. where epidural versus general anesthesia was compared for renal surgeries [15]. Likewise, there is no stronger evidence that support the use of opioids over other drugs in kidney impairment due to potent active metabolites negative feedback. Epidural analgesia is reported to be effective and without significant complications in a limited series [16]. The combination of local epidural anesthetic and opioids has been shown to provide reduction in postoperative pulmonary complications following major abdominal surgeries [17]. Theoretically risks of epidural catheter analgesia in kidney transplant patients results from the common coagulation disorders (platelet dysfunction predominately), cardiovascular comorbidities, fluid shifts and hypotension and reduced graft perfusion. Many patients are requiring postoperative supportive anticoagulant drugs for optimizing graft survival and patients with cadaveric kidney transplant who may suffer from acute tubular necrosis often need post-transplant dialysis due to good long-term outcome and require heparinisation [5,18]. In our observation, one patient had hemorrhage in the surrounding area of the catheter and it was removed on the second postoperative day. Results from our analysis showed a statistical significance in attaining analgesia for the first 2 h in favor of E group. With reference to the other time intervals, no statistical significance was noticed between the groups measured by VAS scale. Patients had satisfactory analgesia at rest and on movement. Similar results have been reported in the literature and there is no consensus proposing one method over another [4,5,15]. One recently published study has reported benefits for graft function in the kidney donor patients who received epidural analgesia. However, the recipients received only general anesthesia and the study had many limitations [19]. Morkane *et al*. stated that the use of paracetamol as an acute painkiller should not be forbidden [5]. Our study results showed that paracetamol was a drug of choice for our anesthesiologist. It provided good analgesia and was safe to be used except in patients who have liver dysfunction. Only four patients from G group required an additional opioid analgesia drug. It is important to say that most of the group G patients received only one dose of medication for the period of 24 h. In-group E, except in one patient, continuous infusion on epidural catheter was discontinued before 24 h and the patient did not ask for additional analgesia. We assume that this was due to the narrow incision in lower abdomen and superficial placement of the transplanted kidney. Therefore, a question should be addressed; is invasive neuraxial epidural analgesia necessary in patients with end stage kidney disease who underwent kidney transplant surgery? Debates over perioperative and postoperative pain management are evident in continental Europe, with ongoing discussion and investigation [20].

This study has a number of limitations that could be applied to future research. First, because this is a single-center study, generalizability is limited. The sample was not randomized, and analgesia was managed according to the anesthesiologist in charge preferences. There is also lack of long postoperative follow-up to evaluate whether there are other late-onset complications. Number of investigated subjects is low.

Conclusion

The study highlighted the variety in clinical practice regarding anesthesiologist preferences for pain management in kidney transplant recipients. This evaluation did not show any difference between anesthetic techniques and clinical results. However, probably epidural analgesia is probably not preferred choice due to invasiveness in the overall low pain intensity.

Kidney transplant recipients are a non-homogenous group of patients with different medical pre-transplant

health history and multiple comorbidities. Therefore, personalized anesthetic technique approach is recommended.

Conflict of interest statement. None declared.

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Case report

Reactive CMV Colitis in Multimorbidity Patient with Ganciclovir Resistance- Post-COVID-19: A Case Report

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Abstract

COVID-19 disease mainly causes mild upper respiratory diseases in infected people, with possible development of complications in 20% of the cases. The virus's predominance for bronchial epithelial tissue and reactive immune response to the virus can result in an overall immune reaction that can trigger latent infections such as cytomegalovirus (CMV) infection or cause bacterial, fungal, or viral coinfections. CMV infection can predispose to other viral respiratory infections, and chronic CMV infection state has been associated with impaired humoral immune response. An abundance of CMV IgG antibodies rate has even been correlated with a higher mortality rate. This state can occur due to underlying immunocompromised status (e.g., undergone transplantation or autoimmune disease) or comorbidity-relations susceptible to the development of complications (such as greater age and underlying chronic diseases), even in a post-COVID-19 state.

Keywords: CMV colitis, ganciclovir, kidney transplant, hypercoagulability, post-COVID-19

Introduction

COVID-19 causes predominately acute respiratory distress with a high possibility of complications and death outcomes in high-risk groups [1]. SARS-CoV-2 has a high affinity for angiotensin-converting enzyme 2 receptors (ACE2), mainly expressed on the epithelial cells lining the bronchial alveoli, what may explain the etiology of respiratory symptoms [2]. Infected patients usually have a mild disease. However, 20% will develop complications due to their predispositions such as age, sex, comorbidities, and overall immune competence [3]. The immunomodulatory effects of COVID-19 on humans have several pathways. The immune system reacts in a defense-based protective way but also exhibits a reaction to the inflammation-driven damaging phase of infection. Immune response takes toll due to various pathophysiologic reactions, such as affection of secondary lymphoid organs, mononuclear cell infiltration, elevation of inflammatory cells, B and T cell lines exposure, high cytokine production, altered coagulation pathways with elevated d-dimers, and many more [2, 4]. This overall reaction to the pathogen can also trigger some latent infections, such as cytomegalovirus (CMV) infection, which can cause colitis with ischemic and inflammatory lesions, which is the case we present in this report. This extensive and complex reaction to the virus brings into question the possibility of immune interference that could explain the age and comorbidity-relations in susceptibility to developing complications and possible concurrent coinfections or reactivations, even in a post-COVID state [5,6].

Case report

We present a case of a 59-year-old woman with many comorbidities, a plentiful medical history, and several prior hospitalizations. Since 1990 she was suffering from recurrent urinary tract infections (UTIs). In 2005, she was diagnosed with polycystic kidney disease and was started on hemodialysis. She received a renal allograft from a deceased donor in 2005 and was maintained on cyclosporine, mycophenolate mofetil and prednisone. Several months after transplantation, the patient had developed iatrogenic diabetes mellitus and massive bilateral pulmonary embolism (PE). She had a prior history of positive serological findings for CMV, for which she has been prescribed a prophylactic dose of valganciclovir. Since 2014, renal allograft function showed signs of impairment with recurrent UTIs, fever, elevated creatinine, and supraventricular tachycardia. Cardiologic workup showed no signs of peripheral arterial disease, ischemia, or myocardial scarring. However, kidney biopsy showed signs of secondary focal segmental glomerulosclerosis (FSGS). Other comorbidities are metabolic syndrome, post PE status (for which she was given low-molecular weight heparin), and subtotal parathyroidectomy. During her frequent relapses of UTI (most common pathogens: Pseudomonas a. or Klebsiella

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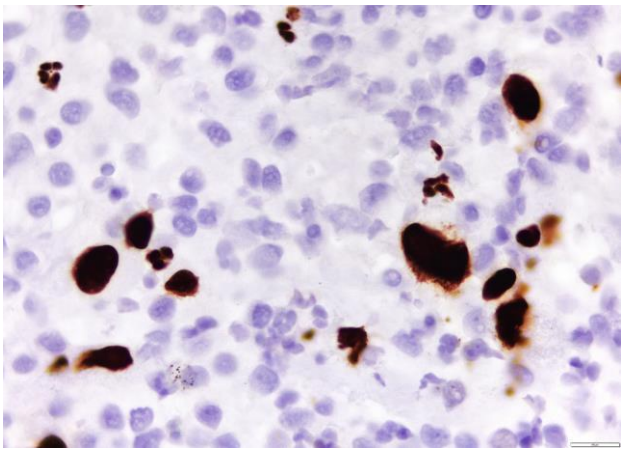
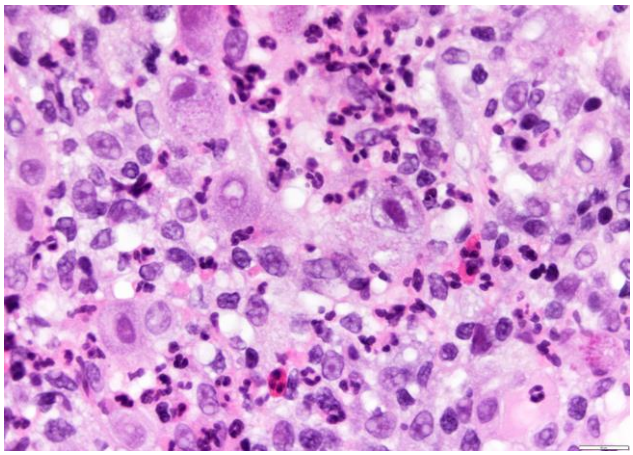
p.), she developed resistance to ciprofloxacin. In 2019, laboratory examination showed detectable quantitative CMV DNA in her blood (1170 IU/mL), so a valganciclovir was introduced to the therapy. Due to her repetitive UTIs, reduced renal allograft function, and CMV reactivation, our patient eventually received ganciclovir, ceftolazane + tazobactam (for UTI), and anti-CMV immunoglobulin (for CMV reactivation). The therapy was working well- the patient's urine was sterile and laboratory results showed normalization of inflammatory parameters and serum creatinine, together with a drop in copies of CMV DNA (<137 IU/mL).

In November 2020, the patient tested positive for SARS-CoV-2. She was hospitalized with the mild form of disease and did not require oxygen therapy.

At the outpatient visit in March 2021, a drop in serum hemoglobin was recorded (from 98 g/L to 56 g/L) with a history of gastrointestinal bleeding. She received a blood transfusion and had undergone esophagogastroduodenoscopy and colonoscopy. The procedure results showed segmental transversal colitis with ulcerations, changes in the mucosa, and diverticula. It also implied possible diverticular or angiodysplastic sources of bleeding. Histologic findings confirmed CMV infection in ulcer tissue. Regular workup revealed normocytic anemia and a new rise in CMV copies to 40100, so ganciclovir and anti-CMV immunoglobulin were prescribed, unfortunately, without therapeutic effect on high CMV reactivation. Drug resistance testing proved resistance to ganciclovir, so foscarnet was introduced to therapy. The new therapy reacted well to high CMV-DNA levels; however, the patient had developed neurologic side effects such as dizziness, headache, disorientation, and hallucinations. The symptoms receded after withdrawal of the drug. The patient is doing well now and was successfully released from the hospital. Letermovir was introduced as a secondary prophylaxis of CMV infection.



A. Hematoxylin eosin staining. Arrows point to specific findings in CMV, inclusion bodies



B. Immunohistochemistry staining for CMV. Arrows point to CMV-specific antigen-stained cells

Fig. 1. Pathohistological findings in colon tissue after intestinal biopsy

Discussion

This complex case of reinfection with latent CMV in older, immunocompromised patient brings into question the immunomodulatory ways of the SARS-CoV-2 virus and possible previous infections and the way they could affect each other. Our patient had a previous immunocompromised state due to an allograft kidney transplant in 2005. Since then, she was on immunosuppressants. She suffered from relapsing UTIs that disturbed her urinary bacterial flora and CMV reactivations, both of which worsened her overall immunocompetence. Most prominent CMV reactivation had developed clinical signs of gastrointestinal bleeding. That was the reason for extensive workup with colonoscopy and colon tissue biopsy. Examination revealed ulcerations, edema, and friability of the mucosa. CMV colitis has been reported in several entities, from thickening of the bowel wall to different etiological states as ischemic, infectious, and inflammatory presentation [5,7].

The immune response to COVID-19 is an acute and dynamic reaction with pro-inflammatory increased cytokine expression, especially in severe cases. It was observed that COVID-19 infection leads to subsequent apoptosis of T lymphocytes, along with loss of $CD4^+$ and $CD8^+$ lymphocytes due to tissue sequestration and excessive production of pro-inflammatory cytokines. All of mentioned could result in the impaired immunological response to pathogen and possible reactivation of latent viruses. Increased vulnerability to targeted organs in COVID-19 could also be explained by the fact that a higher concentration of ACE-2 receptors can be found in the colon, kidneys, liver, vascular endothelium, and others [4,6]. CMV infection could also predispose to respiratory viral infections. Chronic CMV infection has been associated with impaired humoral response, and high CMV IgG antibodies were, in some cases, correlated with higher mortality [8]. Notably, reported cases of concomitant CMV reactivation and COVID-19 infections were all described in patients with turbulent COVID-19 symptoms. However, due to the severe immunocompromised patient in our case,

we conclude that even a mild form of COVID-19 infection can potentially cause reinfections with inflammatory clinical manifestations.

Conclusion

COVID-19 affects predominately upper and lower airway trucks; however, it can also infect other organ systems, including the gastrointestinal tract. This immune disturbance can sometimes, especially in elderly and immunocompromised patients, cause coinfections or reinfections that could further deteriorate the clinical state. Cases of SARS-CoV-2 and CMV coinfections have been reported several times [6,8]. This challenging and extensive case we have presented makes diagnostic and therapy decisions challenging to handle due to several comorbidities, resistance to antiviral drugs, and complex regular therapy as a consequence of the patient's chronic diagnoses and transplant status.

Conflict of interest statement. None declared.

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Case report

Challenges of Deceased Kidney Transplantation in a Patient with Iliac Vein Thrombosis: Case Report

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Abstract

Kidney transplantation is the preferred method of treatment for patients with end-stage kidney disease. A standard surgical technique uses the external iliac vessel for vascular anastomosis. However, sometimes due to the multiple vascular access patients may develop thrombosis and/or stenosis of the iliac vein leading to a challenge in identifying an appropriate vessel for anastomosis and regular graft function. In these circumstances, a multidisciplinary team approach is necessary for optimizing the engraftment survival and decreased morbidity and mortality. Hereby, we present a deceased donor kidney transplantation in a patient with iliac vein thrombosis and discuss facts from the literature.

Keywords: kidney transplantation, iliac vein thrombosis, vein anastomosis

Introduction

Since 1977 until today, in our country kidney transplant has been the treatment of choice for patients with end-stage kidney disease (ESKD) [1,2]. A standard surgical procedure uses the recipient's external iliac vessels for vascular anastomosis [3]. In contrast to the living donor kidney transplantation, in deceased donor transplantation we are facing limited time for the recipient's preoperative preparation. Under these circumstances, thrombosis and/or stenosis of the iliac vein (due to numerous vascular accesses for dialysis), can be found intraoperatively, presenting a surgical challenge. In these cases, different and suitable venous drainage for the renal outflow has to be identified and anastomosed. A multidisciplinary team approach is required for the enhancement of graft function/survival and prevention of complications. We present venous anastomosis in kidney transplant from a deceased donor in the collateral vessel of external iliac vein while iliac vein thrombosis was detected intraoperatively.

Case report

We present a 40-year-old ESKD male patient on dialysis for 4 years. The patient had a positive history for various difficulties with dialysis vascular accesses. Three years ago, an attempt for kidney transplantation from a

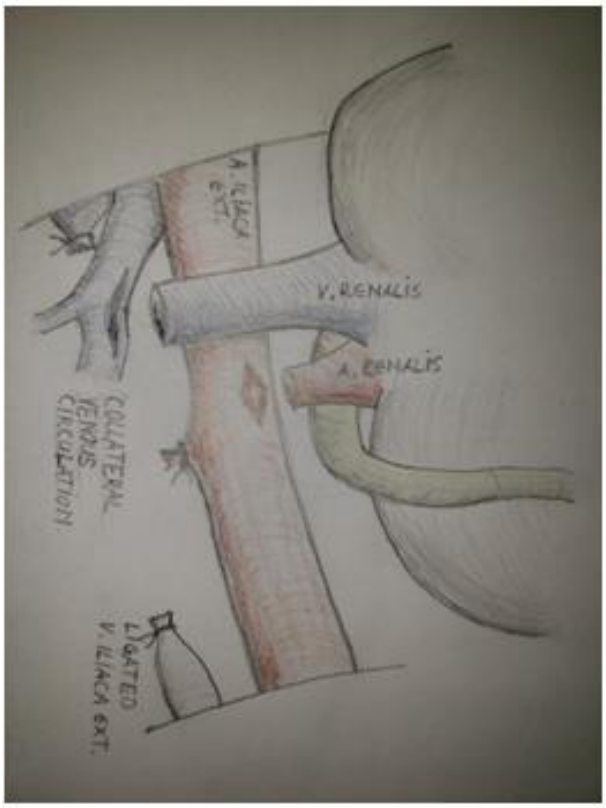

Fig. 1. Sketch of the vessel anastomosis

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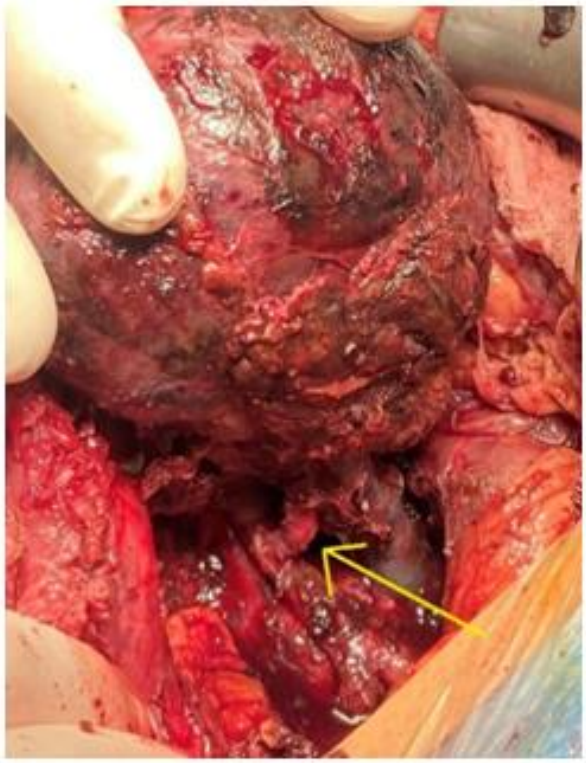

Fig. 2. Intact arterial vascular anastomosis

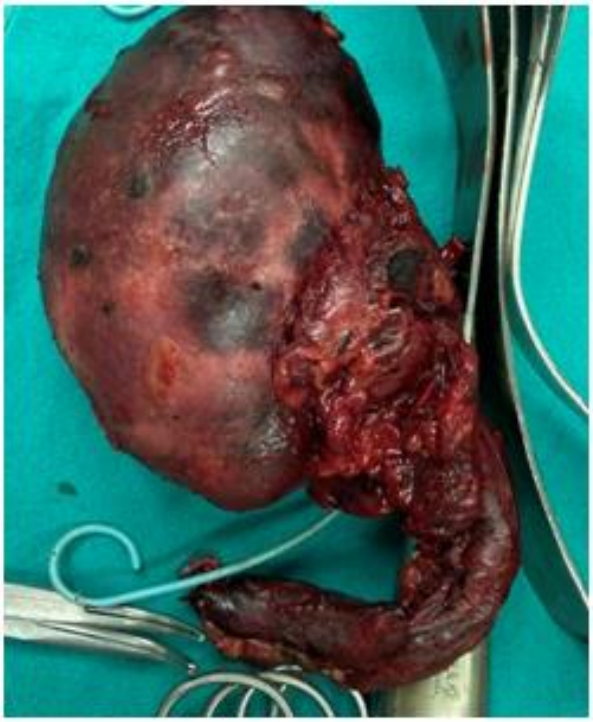

Fig. 3. Kidney necrosis

living donor failed because of severe orchiepididimitis and graft thrombosis. Thereafter, the patient was on therapy with pentoxyfilline due to deep vein thrombosis of the right leg and relatively prolonged aPTT. He underwent his second kidney transplantation from a deceased donor. The left kidney was transplanted in the left side due to a previous surgery on the right side. Induction in anesthesia went uneventful. The surgical dissection was made in the lower abdominal structures. Unfortunately, the surgical team noticed thrombosis of the iliac vessels as a consequence of multiple vascular accesses for hemodialysis, up to the inferior vena cava. A few hours later, one big collateral vein of the external iliac vein was identified, and prepared for venous graft anastomosis (Figure 1).

After 15 hours cold ischemia time and 74 minutes warm ischemia time, the arterial anastomosis and collateral vein anastomosis were finished and the clamp was removed. Unfortunately, not suitable venous drainage led to kidney rupture in the first 5 minutes, although the first urine drops were obtained at three minutes after removing the clamps. Bio glue and absorbable hemostatic surgicel bag were used for surgical hemostasis in one hand, and in the other hand, a systemic anti-fibrinolytic drug (tranexamic acid) 1.5 gr in bolus and 1 gr continuously for 8 h, two units of fresh frozen plasma and 2.5 ml protamine for neutralizing the heparin were administered. Nitroglycerin was administered as well, for vasodilatation and improved venous drainage. All of the above mentioned undertaken safety measures have led to satisfactory hemostasis and graft flow. With satisfactory pulsatile Doppler signal on arterial flow (due to surgical bag obstacles) with adequate urine drops, the surgery was accomplished after 630 minutes. The patient was extubated at the end of the surgery and transferred to the transplant unit. He was hemodynamically stable, although with oliguria since the very first P.O. day. At the third postoperative day, CT-angiography showed thrombosis of the graft. The patient was then transferred to the operating room. Arterial anastomosis was intact, but due to the compromised venous drainage the graft was lost and nephrectomy was performed.

Discussion

Studies show that mortality rate among recipients of kidney transplant is decreased compared to patients on the waiting lists [4]. Many studies are focused on the risk factors for graft loss and patient death in the early post-transplant period [4]. Also, it's known that HLA antibodies are an independent risk factor for graft lost or mortality during the first year after kidney transplant [5,6]. Our patient had HLA sensibilization due to the previous transplant from a living donor. According to the literature, other risk factor associated with graft lost is the cardiovascular condition of the deceased donor [6,7]. Studies showed that arrhythmia and left ventricular ejection fraction lower than 56% were independent risk factors for early graft failure or mortality [7-9]. Until today, there is no known recommendation for cardiovascular screening in kidney transplant recipients,

since there is a lack of evidence from randomized clinical trials [8,9]. We presented the case of a 40-year-male patient without any known cardiac comorbidities. Before the surgery, the patient had intraoperative and postoperative normal findings on ECG and good left heart contractility.

In the literature there are 1 to 18% reported complications of all kidney transplants related to the surgical technique of vascular anastomosis [10]. The complications are often reported in the right-side kidney transplant, although in our presented case we had a left side kidney transplanted on the left side. Another complication emerges from the short vessels that lead to prolonged warm ischemia time during vessel anastomoses. Cases of recipients with vein thrombosis have been reported in the literature [10,11]. Our patient also had thrombosis of iliac vessels all the way to vena cava inferior due to multiple dialysis catheters in the left femoral vein. Efforts to anastomose renal vein with inadequate vein will probably result in irregular anastomosis that will be angulated, under pressure or with inadequate flow. Without any other possible solution, we decided to anastomose the renal vein with one collateral vein branch of the recipient's external iliac vein. At the same time, we were aware of the possible technical problems like thrombosis or hemorrhage that may lead to a graft failure. In the literature saphenous autograft, gonadal vein, bovine heterograft or vascular prosthesis have been reported for vessel anastomosis with good results [10,12,13]. Cerqueira *et al*. reported a successful graft survival in five cases with thrombosis and/or stenosis of iliac vein anastomosed with gonadal vein. In three cases, they reported a delayed graft function; two cases had infection and one patient was re-operated [13]. The presented case was medical emergency due to impending inability of establishing vascular access for dialysis. Due to thrombosis, iliac vessels or inferior vena cava was not a suitable option and the best available alternative was chosen. Unfortunately, we did not achieve satisfactory drainage with the obtained vein graft anastomosis and the third postoperative day the graft was lost. We assume that constrained vascular anastomosis with poor vascular condition related to possibly disordered coagulopathy should be the reason for early graft lost in the presented case.

Conclusion

Venous anastomosis with collateral iliac vein, for kidney transplantation in patients with iliac vein thrombosis gives usually good results. This method may be used as a satisfactory alternative for venous drainage in complex cases like ours. In cases with multiple catheter insertions or waitlisted candidates for re-transplantation, recent angiography images are required, in order to be considered as possible cadaveric kidney recipients.

Conflict of interest statement. None declared.

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In memoriam

"Bantao Journal is a Strong Glue Among Nephrologists from the Balkan Cities!" Momir H. Polenakovic (1939-2021)

Goce Spasovski

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The nephrology and especially BANTAO community has lost one of its pioneers and founders, Professor Momir Polenakovic, MD. Prof. Polenakovic passed away at the University Hospital in Skopje, North Macedonia at the age of 82. Prof. Momir Polenakovic was born on April 26th, 1939, in Skopje and died on March 6, 2021 after having acutely suffered from severe COVID bronchopneumonia. The nephrological community expresses its deepest sympathy to his wife Biljana and his sons Radmil and Hari. His colleagues, students, peers, and patients will miss a dedicated physician and thorough clinical scientist with wide recognition in the area of clinical and preventive nephrology, a teacher and a passionate writer about the national and regional history of nephrology.

Dr. Polenakovic graduated from the Medical Faculty of the Ss. Cyril and Methodius University in Skopje and received an MD degree in 1963. His further studies at the Clinic of Internal Medicine and Nephrology in Skopje, as well as at the Military Medical Academy in Belgrade, Serbia, Northwestern University in Chicago, and Harvard Medical School, Boston, USA, were dedicated to internal medicine with a focus on nephrology and nephroimmunopathology.

He defended his thesis: "Clinical and immunological evaluation of pathological events in renal glomeruli", becoming an Assistant Professor at the Medical Faculty, University Sts. Cyril and Methodius, Skopje in 1977.

He was elected as Vice Dean of the Medical Faculty, University Sts. Cyril and Methodius, Skopje from 1982-1984. He also became an Associate Professor in 1983 and a Full Professor in 1988 of internal medicine at the Medical Faculty of the University Ss. Cyril and Methodius, Skopje.

Prof. Polenakovic was the Head of the Department of Nephrology from 1990-1997, and in 1997 was elected as a member of the Macedonian Academy of Sciences and Arts. He was also its Vice President during the term of 2004-2007.

From 2011-2017, Prof. Polenakovic was the Head of the Research Centre for Genetic Engineering and Biotechnology "Georgi Efremov" of the Macedonian Academy of Sciences and Arts.

Since his retirement in 2005, he continuously worked in field of the medicine, publishing papers and contributing to the medical sciences as Macedonia's most fruitful medical scientist, with 228 Medline cited articles. His research interests encompassed glomerulonephropathies, tubulointerstitial diseases (especially Balkan endemic nephropathy), diabetic nephropathy, polycystic kidney disease, chronic renal failure, dialysis, and plasmapheresis.

He was a collaborator of many international trials, and, in fact, provided our country with the first opportunity to participate in the successfully conducted study on erythropoietin in the 1990s.

Prof. Polenakovic was the founder of the Macedonian Society of Nephrology, Dialysis, Transplantation and Artificial Organs (MSNDTAO) in 1992, and also a co-founder of the Balkan Association of Nephrology, Dialysis, Transplantation and Artificial Organs

(BANTAO) in 1993 and its President from 1997-1999. He promoted the idea that the BANTAO association was the regional web that maintained its cohesion through cooperative science for the good of our patients, borderless and without political influence. Hence, he was the organizer of many international congresses, and the European and International Nephrology Society supported many of his CME courses. His warm hospitality and splendid organizational skills were recognized and respected by scientists and friends alike from all over the world.

The international recognition of Prof. Polenakovic and his efforts to secure support for many young colleagues for their international education helped him to develop a team of collaborators who will continue his ideas and further advance the field of the nephrology in the region.

Finally, one of Prof. Polenakovic's greatest achievements was the promotion of the journal Prilozi to be accepted at the most visible medical database, Medline, and thus, papers with domestic authors can now be discovered online for international research. Prof. Polenakovic received many international awards and charters including the First ISN Pioneer Award for the Eastern and Central Europe Region.

We will certainly miss our leader, teacher, and shining example of an outstanding scientist and caring physician for many patients. Yet, we will also miss a friend, whose delicate and helpful words of wisdom were ready at each consultation. From a nephrology pioneer to a regional leader, Prof. Polenakovic was dedicated to the improvement of nephrology via mutual scientific collaboration across borders. He was a man with an open heart and unparalleled hospitality, whose goal it was to spread the spirit of free communication of science across borders.

Let him rest in piece and his achievements stay forever!

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The 16th Congress of the Balkan Association of Nephrology, Dialysis, Transplantation and Artificial Organs (BANTAO)

Abstract Book

29 - 31 October, 2021, Tirana, Albania

Oral presentations

OP-01 Morbidity and mortality rate in hemodialysis patients with CoVid-19

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Introduction. Patients with end stage renal disease on hemodialysis (HD) are burdened, amongst all well-known comorbidities, with an impaired immunological defence towards large number of infectious diseases. In parallel, corona virus disease 2019 (COVID-19) pandemic has brought further challenges for the medical professionals providing maintenance hemodialysis in safeguarding the patients while providing clinical care.

Methods. Retrospective analysis was conducted in a single HD center during period of 12 months, from October 1, 2020 till September 30, 2021. Patients' demographic and clinical characteristics were analyzed for morbidity and mortality risks.

Results. Out of the 207 patients who were treated during the observational period, 47(23%) patients were affected by COVID-19, 20(42.6%) females and 27(57.4%) males at mean age of 67.3±10.9 years. The hospitalization rate among patients with COVID-19 was 38.2% and the overall mortality was 28% (72.2% in hospitalized patients). There was significance regarding age (p=0.04) for increased mortality, but not hospitalization. Sex of the patients showed no significance in hospitalization (p=0.89) and mortality risks (p=0.74). Charlson comorbidity index in the study population was 6.6±2.9, but was significantly higher in hospitalized patients 7.8±3.1 (p= 0.03) and died due to COVID-19 (p=0.004). Karnofsky score was 70.4±18.4%, and showed no significant impact in hospitalization 64.71% (p=0.06) and mortality rate 66.67% (p=0.21).

Conclusion. Morbidity and mortality risk in HD patients affected by COVID-19 are higher than for the general population. In our cohort, age was associated with an increased risk for morbidity and mortality, and sex of the patients' had no influence. However, COVID-19 patients who were hospitalized or died had higher Charlson comorbidity index.

OP-02 Nonadherence to dietary and fluid program among patients undergoing haemodialysis

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Introduction. For end-stage renal disease (ESRD), patients on a hemodialysis (HD) nutritional regime focusing on diet and fluid intake is recommended. Nonadherence to the suggested program is associated with worse outcomes.

Methods. This cross-sectional survey was conducted to determine the prevalence of nonadherence to the dietary and fluids restrictions among ESRD on HD patients during March-April 2021. Each participant was interviewed and their medical records reviewed to obtain relevant socio-demographic and clinical data. The mean inter-dialytic weight gain (IDWG) was calculated for one month prior to the date of a questionnaire for each patient. NA to fluid restriction was defined as a mean IDWG in the past month >5.7% of the dry weight, NA to dietary restriction as a predialysis serum phosphorus >5.5 mg/dl in a patient on phosphate binders and who is well-nourished.

Results. A total of 81(67% male) HD patients were included. Mean age was 53±12 years (range 22-77); The median dialysis vintage 6.2±3.9 years; Mean Body Mass Index (BMI) 24.5±3.9 kg/m2; mean IDWG 3.03±0.8 kg; mean serum albumin level 3.9±0.3 g/dl; mean serum phosphor level 5.4±1.4 mg/dl. NA prevalence was (13/81) 16% to fluid restriction, (39/81) 47.6% to dietary restriction. According to each patient interview, only 7% find it impossible to follow the fluid restriction program, and (26) 32% to dietary restrictions. Comorbidity (arterial hypertension and diabetes mellitus) were independently associated with NA to dietary restrictions (OR: 3.46, 95% CI: 0.99-12.11; p=0.052). No factor was associated with NA to dietary restrictions and HD sessions.

Conclusion. Regular counseling to HD patients and family members according to diet and fluid restrictions program is needed, especially for patients with comorbidities.

OP-03 Sleep disturbance, depression and anxiety in hemodialysis patients in COVID-19 pandemic

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Introduction. COVID-19 has not only threatened physical health but has also grown as a burden on public health, economics, and mental well-being. We aimed to assess symptoms of anxiety, depression, and sleep disturbances among HD patients during the COVID-19 pandemic and determine factors associated with psychological distress.

Methods. In this observational, cross-sectional study, HD patients were asked to fill out a questionnaire about socio-demographic factors, education level, employment and economic status, and marital status. They were asked about worries regarding the COVID-19 infection,

whether COVID-19 had infected them, admitted to hospital, or the ICU. Each participant was delivered Pittsburgh Sleep Quality Index (PSQI), Beck Depression Inventory (BDI), and Beck Anxiety Inventory (BAI).

Results. The mean age of 58 patients was 50.9±14.6 years, and 29 (50%) were males; 19 (32.8%) had been infected with COVID-19, and 10 (15.5%) were admitted to the hospital. Fifteen patients had household contacts who had been infected with SARS-CoV-2, and four patients had household contacts who died. Most (69%) have reported unaffected by the COVID-19 news, while 29% have said that media increased their worries. 77.6% have reported that they were unemployed, and seven (12%) have either lost their jobs or were negatively affected. Sleep quality was poor (PSQI≥5) in majority (n=36,59%). Having COVID-19 was found to harm sleep quality. Poor sleep quality was seen in 68.4% of COVID-19 survivors, whereas this ratio was 59% in participants for whom SARS-CoV-2 had not been infected.

Conclusion. The pandemic has affected the lives of HD patients in health, social, or economic respects. The sleep quality seems to be negatively influenced by COVID-19.

OP-04 Are C4D, nephrin, and wt1 expressions important in the differential diagnosis between focal segmental glomerulosclerosis and minimal change disease

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Introduction. Focal Segmental Glomerulosclerosis (FSGS) and Minimal Change Disease (MCD) is the most common seen glomerulonephritis. Differential diagnosis between FSGS and MCD by light microscopy cannot be made at some time and electron microscopy (EM) is needed for differential diagnosis. However, in some cases, EM may not be sufficient for differential diagnosis. A new marker needed to diagnose FSGS and MCD This study aims to determine which of the glomerular C4d, nephrin staining is specific and sensitive for FSGS and MCD.

Method. The retrospective study included patients with FSGS, MCD who could not differentiate between FSGS and MCD. The patients were divided into three groups. Group 1: FSGS patients, Group 2: patients with normal IM but whose difference between FSGS and MCD could not be differentiated, and group 3: MCD patients. All biopsy materials of all patients were stained with C4d, WT1, nephrin. The specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV) of C4d, WT1, nephrine in the diagnosis of FSGS and MCD were evaluated.

Results. C4d staining in group 1 was significantly higher compared to group 2 and group 3 ($p<0.05$). Nephrin was showed significantly more staining in group 3 patients than group 1 ($p<0.05$). C4d was found to be associated with the presence of global or segmental sclerosis in the glomeruli, adhesion to the Bowman's capsule ($p<0.05$). The specificity and sensitivity of C4d in FSGS patients were 85%, 73.9%, while it was 26.1% and 15.4% in MCD. Specificity and sensitivity of nephrin were 87%, 69% in MCD patients compared to 30.8% and 13% in FSGS.

Conclusion. C4d and nephrin stanning appear to be very valuable in the differential diagnosis of FSGS and MCD. Studies with a large number of patients are needed in this regard.

OP-05 Eosinopenia and lymphopenia as predictor of poor outcome in dialysis patients with COVID-19

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Introduction. The COVID-19 pandemic affects more aggressively patients with comorbidities, including dialysis patients. This study aims to identify severity and mortality markers and respective cut-offs in this group of patients.

Methods. We used the receiver operating characteristic (ROC) curve to produce sensitivity, specificity, and cut-off values. All chronic dialysis patients getting treatment in a single-center, Hygeia-Hospital-Tirana.

Results. 52 out of 170 dialysis patients were diagnosed with Covid-19. The mean age 61.5±12.3 years, 65.4% men. The prevalence of Covid-19 in dialysis was 30.5%, with mortality rate of 19.2%. Mortality rate was higher in Diabetic Nephropathy patients ($p<0.04$) and in patients with Peripheral Vascular Disease ($p<0.01$). Risk factors for severe disease were high BMI ($p< 0.024$), high RDW ($p<0.03$), high C-reactive protein ($p<0.018$), high ferritin ($p<0.021$).

ROC curves identified lymphopenia and eosinopenia, as markers of severity and mortality.

Cut-offs were chosen for Eosinopenia (EO), exitus (0.185%); Lymphopenia (LYM) exitus (13.15%); LYM severity (15.70%), and EO severity (0.31%).

Conclusion. We found eosinophils and lymphocytes in inverse relationship to the poor outcome of Covid-19 in dialysis patients. Therefore, must be aware of the

Table 1. Eosinopenia and lymphopenia in dialysis patients with COVID-19

	AUC	Asymptotic 95% Confidence Interval Lower Bound	Asymptotic 95% Confidence Interval Upper Bound	Positive if Greater Than or Equal To[a]	Sensitivity	Specificity
EO % severity	0.786	0.633	0.938	0.3100	0.739	0.643
LYM % severity	0.825	0.692	0.957	15.7000	0.793	0.778
EO% exitus	0.814	0.613	1.000	0.1850	0.727	0.750
LYM% exitus	0.739	0.510	0.969	13.1500	0.800	0.857

trend of eosinophils and lymphocytes at dialysis patients infected by Covid-19 because if these two markers are progressively worsening, it indicates a higher chance of poor outcome and a high mortality rate among them.

OP-06 COVID-19 infection in kidney transplant recipients: a single center experience

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Introduction. Kidney transplant recipients appear to be at exceptionally high risk for critical COVID-19 illness due to chronic immunosuppression and coexisting conditions. This study aims to present the clinical characteristics and outcomes of our hospital kidney transplant recipients hospitalized due to COVID-19 infection.

Methods. In our retrospective, observational study, COVID-19 PCR positive 20 patients hospitalized with COVID-19 pneumonia were evaluated with demographics, laboratory data, treatment, and outcome. The prognostic nutritional index (PNI) calculated using the serum albumin concentration, and total lymphocytic count were also evaluated. All patients were treated with favipiravir+low molecular weight heparin; laboratory tests were recorded before and after favipiravir treatment.

Results. Of 20 patients, 12 were male. A total of 12/20 (60%) patients survived. All patients were treated with favipiravir; laboratory tests were recorded before and after favipiravir treatment. The clinical parameters of patients are shown in Table-1 and Table-2. The mean PNI of the patients who survived was higher than patients who were exits.

Conclusion. The eight patients who died were older, had lower PNI and higher NLR (Neutrophil/Lymphocyte Ratio), procalcitonin, and CRP levels. Hospitalized kidney transplant recipients with COVID-19 have higher rates of mortality. PNI on admission exhibited good predictive performance and may be a useful clinical marker that can be used for estimating survival in COVID-19 patients.

Table 1. Clinical and laboratory findings of patients at the time of hospital admission

	Discharged n= 12	Dead n=8	p
Age	45.2±12.7	60.6±10.3	0.011
Gender (male/female)	8/4	4/4	0.648
Lenght of hospital stay (day)	7 (1-12)	15 (8-25)	0.057
PNI	43.8 (37.8-48.3)	36.7 (34.8-38.5)	0.043
WBC, $x10^9$/L	5.8±3.58	7.28±5.41	0.427
Neutrophil, $x10^9$/L	3.82 (2.24-5.37)	5.22 (2.49-7.93)	0.305
Lymphocyte, $x10^9$/L	0.96 (0.64-1.25)	0.44 (0.25-0.96)	0.157
Creatinine, mg/dL	1.24 (0.96-2.28)	2.35 (1.73-4.12)	0.123
NLR (Neutrophil/Lymphocyte Ratio)	5.56 (2.66-8.52)	11.25 (6.91-23.27)	0.020
Hemoglobin (g/dL)	14.0±1.79	11.3±1.17	0.005
LDH, U/L	254 (205-274)	256 (197-522)	0.515
Troponin T, ng/mL	0.017 (0.013-0.028)	0.041 (0.027-0.062)	0.006
Procalcytonin, ng/mL	0.091 (0.052-0.104)	0.345 (0.207-1.118)	0.008
Ferritin, ng/mL	462 (192-1060)	895 (395-2000)	0.238
D-dimer, µg/L	335 (198-484)	348 (266-407)	1.000
CRP, mg/L	17.5 (7.2-41.9)	59.0 (41.4-111.5)	<0.010

Table 2. Laboratory findings of the patients after favipiravir treatment

	Discharged n= 12	Dead n=8	p
PNI	45.4 (35.3-56.9)	26.5 (22.6-31.3)	0.003
WBC, $x10^9$/L	6.91±1.64	12.57±9.98	0.082
Neutrophil, $x10^9$/L	4.87 (4.14-6.07)	10.96 (4.67-12.93)	0.069
Lymphocyte, $x10^9$/L	1.11 (0.96-2.00)	0.40 (0.17-0.80)	0.005
Hemoglobin (g/dL)	13.8±1.89	10.1±1.53	< 0.0001
NLR	6.88 (4.49-7.72)	21.39 (8.73-39.01)	0.033
CRP (mg/dL)	10.9 (5.4-21.2)	96.0 (63.3-302.8)	< 0.0001
Creatinin (mg/dL)	1.03 (0.92-1.81)	2.96 (1.52-3.79)	0.012
LDH, U/L	275 (213-366)	513 (351-799)	0.011
Troponin T, ng/mL	0.017 (0.013-0.045)	0.103 (0.073-2.313)	0.004
Procalcitonin, ng/mL	0.056 (0.039-0.085)	1.450 (0.152-4.430)	0.006
Ferritin, ng/mL	305 (177-1494)	2000 (963-2000)	0.042
D-dimer, µg/L	1088 (569-2013)	5901 (1335-7771)	0.073

OP-07 Are renal prognostic markers different in patients with exostosin1/2 positive and negative in membranous lupus nephritis? Single center experience in Turkey

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Introduction. Exostosin1/exostosin2 (EXT1/EXT2) are new antibodies detected in MLN and new research are needed on these markers. The aim of this study is to determine whether renal prognostic markers differ in EXT1/EXT2 positive and negative patients with MLN and relationships with these markers.

Methods. Single-center, retrospective 18 months, observational study, class 5 MLN patients aged 18 years and older were included in the study. The outcome of the study was determined as complete remission, partial remission, need for renal replacement therapy (RRT) and exitus. Group 1: EXT1/EXT2 positive, group 2: EXT1/EXT2 negative patients. Light and electron microscopy findings and laboratory parameters were evaluated in EXT1/EXT2 positive and negative patients.

Results. Group 1: n=11, group 2: n=7 patients. EXT1/EXT2 negative patients have a higher number of sclerotic glomeruli, interstitial fibrosis, and a higher amount of proteinuria than positive patients ($p<0.05$). EXT1/EXT2 negative patients had significantly lower C3 and C4 levels than positive patients ($p<0.05$). EXT1/EXT2 negative patients had a higher RRT or exitus rate within 18 months than positive patients ($p<0.05$). In contrast, EXT1/EXT2 positive patients had a higher rate of achieving complete or partial remission within 18 months than negative patients ($p<0.05$).

Conclusion. EXT1/EXT2 negative class 5 MLN patients have more poor renal prognostic indicators than positive patients. RRT or exitus rate is higher in EXT1/EXT2 negative patients than positive patients. However, more randomized controlled studies are needed.

OP-08 May ischemia modified albumin be a predictor in diagnosis of contrast induced nephropathy?

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Introduction. "Ischemia modified albumin" (IMA) was investigated as a possible biomarker in several diseases such as vascular disorders. We aimed to reveal the possible value of IMA in predicting the development of contrast-induced nephropathy (CIN) after coronary angiography in patients with stable angina pectoris.

Methods. 106 patients who underwent coronary angiography with a diagnosis of stable angina pectoris were included in our study. Essential demographic and clinical findings and laboratory values were recorded and analyzed. Serum creatinine (SCre) levels were also measured 48hours after coronary angiography and recorded. Amount of contrast agent (CA) given during coronary angiography was recorded. The patients were divided into Two groups: CIN positive and CIN negative groups.

Results. CIN was developed in 14 patients (13%), and IMA levels were similar in CIN positive and negative groups ($p>0.05$). SCre (both measurements before and after CA administration) was not correlated with IMA levels. There was no association between drug usage and the development of CIN ($p>0.05$). Comorbidities were not associated with the development of CIN ($p>0.05$), except hypertension (HT). The presence of hypertension ($p=0.0393$) and female gender ($p=0.0199$) was associated with the development of CIN. Mean age was 61.3 and 52.3 in CIN positive and negative groups, respectively ($p>0.05$).

Conclusion. Any specific biomarker indicating CIN is not available yet. The most frequently used marker is the measurement of SCre 48 hours after administration of CA. We found IMA levels not to be a predictor for the development of CIN. Further investigations will determine the importance of IMA as a biomarker in renal failure developed after CA administration.

OP-09 Primary and secondary glomerular diseases in university Clinical Center of Republic of Srpska -results of kidney biopsises in period Banja Luka 2007-2021

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Introduction. The study aimed to show the number and pathophysiological diagnoses of patients with glomerular diseases in the University Clinical Centre of the Republic of Srpska in 2010-2021.

Methods. During this period, we performed 326 kidney biopsies under ultrasound guidance. There were 143 women and 183 men; 181 patients were between 18-60 year and 55 patients over 60 years. We performed a kidney biopsy of native kidneys, analyzed with optical microscopy and immunofluorescence. We took a sample for electron microscopy analyzed in Clinical Centre Dubrava (Croatia), due to lack of technical requirements for electronic microscopy in our center.

Results. Indications for biopsy were: nephrotic syndrome 193 patients (53,3%), nephritic syndrome 51 patients (15,6%), asymptomatic urinary abnormalities (persistent proteinuria and/or micro or gross hematuria 43 patients (13,1%), chronic renal failure (unclear cause) 26 patients (7,9%) and acute renal failure 13 patients (3,9%).

Primary and secondary glomerular diseases were diagnosed in 238 patients, primary glomerulonephritis in 138 patients (48%), and secondary glomerulonephritis in 100 patients (34,8%). The other three groups were vascular, tubulointerstitial diseases, and other findings. Primary glomerular disease: membranous GN 44 patients, IgA nephropathy 29 patients, focal segmental glomerulosclerosis 25 patients, minimal change disease 13 patients, membranoproliferative glomerulonephritis 11 patients, mesangioproliferative (non-IgA) glomerulonephritis 11 patients, primary crescentic glomerulonephritis three patients, post-streptococcal glomerulonephritis, two patients.We divided secondary glomerular diseases into three groups (modeled on the Italian registry): Group 1-immune-mediated GN: lupus nephritis 37 patients, ANCA vasculitis 23 patients, Goodpasture syndrome two patients; Group 2-dysgammaglobulinemia associated GN: amyloidosis 13 patients, light chain disease six patients and cryoglobulinemia one patient; Group 3-metabolic and hereditary glomerulonephritis: diabetic nephropathy 16 patients, thin glomerular basement membrane disease one patient and Alport syndrome one patient.

Conclusion. Most frequent diagnoses were: membranous glomerulonephritis in 44 patients, lupus nephritis in 37 patients, and IgA nephropathy in 29 patients.

OP-10 Impact of prolonged hemodialysis on ejection fraction

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Introduction. Chronic heart failure (HF) is highly prevalent in dialysis patients and significantly affects morbidity and mortality. Numerous attempts to treat HF have been investigated by changing hemodialysis (HD) modalities. This pilot study aimed to check whether HD duration could impact left ventricular dysfunction and other applied therapy.

Method. HF was found in 63/96 prevalent HD patients, and they were divided into groups; Group 1-21 patients with reduced EF <50 % (HFrEF); Group 2-42 patients with preserved EF ≥50% (HFpEF), and the third group with 33 patients without HF. HD treatment was prolonged from 12 hours to 15 hours per week for three months in half of the patients in each group. Patients' data were collected from medical records. In addition to routine laboratory analysis, complete lipid status and oxidative stress (OS) were performed. Ultrasonographic examination was performed at the beginning and after the three months of prolonged HD.

Results. HD prolongation resulted in recovering EF >50% in 2/9 patients with HFrEF and worsening EF <50% in 1/21 patients with HFpEF. In subgroups without HD prolongation, five patients with HFpEF worsened EF <50%, and one patient from group 3 developed HFpEF. Antioxidant capacity significantly increased in groups 1 and 3. No other difference was found.

Conclusion. These findings suggest that three hours weekly HD prolongation may have a beneficial effect on EF, especially in patients with HFrEF. OS could mediate this effect.

OP-11 Cresentic glomerulonephritis related to COVID-19 infection: case series

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Introduction. Coronavirus disease 2019 (COVID-19) can lead to kidney damage by many mechanisms. Although it was reported that infection caused an insignificant increase in the frequency of acute kidney injury (AKI) in the early stages of the epidemic, the frequency increased significantly over time, especially in inten-

sive care patients. In genetically susceptible cases, COVID-19 may rarely trigger the production of anti-neutrophil cytoplasmic antibodies (ANCA) against neutrophil serine protease proteinase 3 (PR3) and myeloperoxidase (MPO) enzymes, contributing to the development/ exacerbation of secondary vasculitides. With this article, we would like to draw attention to the glomerular severe damage potential of the virus with rapidly progressive kidney failure (RPGN) cases following COVID-19 infection.

Method. The data of nine patients who developed RPGN during or immediately after COVID-19 infection were evaluated retrospectively. Based on current guidelines, all patients had received pulse steroids, cyclophosphamide, and ± plasmapheresis. Patient characteristics, laboratory data, treatments are presented in Table 1.

Discussion. Acute tubular injury and collapsing glomerulopathy are the most common histopathological findings in COVID-19 cases. However, with the increase in our knowledge about COVID-19 over time, cases of RPGN associated with COVID-19 have begun to report increasingly. COVID-19 infection may be a "triggering factor" for vasculitis. Only a few cases of ANCA-positive RPGN have been reported in the literature. Although previously published case reports showed that COVID-19 might be associated with developing another crescentic glomerulonephritis, we mainly encountered cases with MPO-ANCA positivity. In the differential diagnosis of COVID-19-associated AKI, we should consider crescentic glomerulonephritis and look for clinical and laboratory clues for RPGN.

Patient	Age/Sex	Serology	Bazal sCre (mg/dl)	Peak sCre (mg/dl)	Renal replacement therapy	Covid-admission time (week)	Celuler/ Fibrocelüler crescent %	Kidney pathology	Treatment	Plasmapheresis(session)	Follow up(month)	Final sCre (mg/dl)
1	73/F	p-ANCA	1.05	5.5	-	12	-/38	İmmune complex	Cyc/Aza	+/6	6	2.08
2	54/M	c-ANCA	0.67	4.1	+	12	19/42	Pauci-immune	Cyc	-		1.5
3	65/M	c-ANCA	0.9	4.8	+	6	68/8	Pauci-immune	Cyc	+/7		2.7 (EX)
4	61/M	p-ANCA	0.88	1.6	-	26	12/14	Pauci-immune	Cyc	-		1.2
5	61/F	p-ANCA	1.33	6.18	+	simultaneous	33/20	Pauci-immune	Cyc/Aza	9		2
6	60/M	p-ANCA	1.06	1.88	-	18	60/26	İmmune complex	Cyc	-		1.2
7	33/F	c-ANCA	0.6	4.08	-	Not known*	57/26	İmmune complex	Cyc	+/7	7	0.86
8	82/M	-	1.2	6.40	+	13	62/17	İmmune complex	Cyc	+/7	5	7.2
9	52/F	p-ANCA	0.89	5.56	+	Not known*	37/48	Immune complex	Rtx	+/11	2	4.7

*Covid-19 Ig G antibody positive at the time of admission, Cyc, cyclophpsphamide, Aza, azathioprine; Scre, serum creatinine; ANCA, anti antineutrophil cytoplasmic antibodies

OP-12 Comparison of serum sclerostin level and pulse wave velocity in patients with routine hemodialysis and non dialysis glomerulonephritis patients

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Introduction. Pulse wave velocity (PWV), one of the crucial markers of atherosclerotic disease, and the effect of sclerostin on chronic kidney disease have been shown in many studies. Studies on autoimmune kidney involvement such as glomerulonephritis are very few. Therefore, our study aimed to compare serum sclerostin level and PWV in hemodialysis patients and patients with glomerulonephritis.

Methods. 30 patients undergoing routine hemodialysis and 51 patients with glomerulonephritis proven by kidney biopsy were included. Demographic and clinical characteristics and routine biochemical parameters were recorded from the hospital information system. PWV was determined from the patients using the Mobil-o-Graph NG arteriography device. Serum sclerostin level was measured as pg/ml by the ELISA method.

Results. Thirteen female and 17 male hemodialysis patients and 20 female, 31 male glomerulonephritis patients were included. While the median serum sclerostin value of the whole group was 494.4 pg/ml, it was found to be 2177.7 pg/ml in the glomerulonephritis group, much higher than in the hemodialysis patient (235.5 pg/ml), ($p<0.001$). Pulse wave velocity (PWV) was higher in the glomerulonephritis group and was statistically significant ($p<0.001$). While there was a significant positive correlation between the sclerostin level and PWV and proteinuria, there was a significant negative correlation with age, GFR, creatinine, neutrophil, PTH, neutrophil-lymphocyte ratio.

Conclusion. We found that sclerostin and PWV levels were higher in the group with glomerulonephritis and might be associated with atherosclerosis in glomerulopathies like in HD. In addition, studies conducted in patients with glomerulopathy, albeit very few, have shown correlations between sclerostin and PWV levels and proteinuria, serum complement levels, and inflammation, and they may be clinically useful as a biomarker of disease activity.

OP-12 Peritoneal dialysis-related peritonitis: rate, clinical outcome and patients survival

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Introduction. Peritoneal dialysis-related peritonitis remains the major complication and primary challenge to the long-term success of peritoneal dialysis. The observational study aimed to analyze the peritonitis rate, the cause, the outcomes, and the association of peritonitis with the survival of patients.

Methods. Data were collected retrospectively from the medical charts. A total of 96 patients received peritoneal dialysis in our center from 1 January 1999 to 31 December 2018. The mean age of patients was 46.8±16.4 years, and the mean time receiving peritoneal dialysis was 3.5±3.1 years. The study population was divided into two groups, a group of patients (n=54) who experienced peritonitis and a group of patients free of peritonitis (n=42).

Results. The peritonitis rate was 0.47 episodes per patient-year. The majority of causative microorganisms were gram-positive bacteria (53.5%). Outcomes of episodes of peritonitis were completely resolved infection presented in 135 (84.9%) episodes, catheter removal in 18 (11.3%) episodes, and death in 6 (3.8%) episodes of peritonitis. Kaplan-Meier analysis and log-rank test revealed that there was a significant difference in survival between the groups, the group experiencing peritonitis tended to survive longer than the group that was peritonitis free (P=0.000). The peritonitis was a predictor associated with improved survival of patients, a 67% reduction in the risk of patient mortality was observed for the group experiencing peritonitis compared with the peritonitis free group (hazard ratio: 0.33, 95% CI 0.19-0.57, P=0.000).

Conclusion. The prevention and management of PD-related infections, resulted in their worldwide reduction, supporting the use of PD as a first-line dialysis modality.

OP-13 Kidney injury in thrombotic microangipathy

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Introduction. Thrombotic microangiopathy clinically presents as a syndrome with hematological disorders: low platelets count, hemolytic anemia, and organ damage. While being the injured organs, the kidneys do not show characteristic monoclonal immunoglobulin deposits, but they are damaged through complement activation. The clinical appearance is very severe and life-threatening if not diagnosed and treated promptly. Thrombotic microangiopathy (TMA) was recently classified in the so-called MGRS (Monoclonal Gammopathy of Renal Significance).

Case report. We described a clinical case diagnosed with TMA. It presented with acute kidney injury, low platelet count, anemia, a very severe clinical picture, rapid deterioration toward septic shock. The clinical and laboratory findings, together with kidney involvement, were decisive for further investigations. Hypocomplementemia and ADAMTS 13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13) positivity suggested the TMA diagnosis, kidney biopsy confirmed it. The treatment with complement inhibitors was successful, and kidney function was restored.

Conclusion. The renal involvement in acute and severe clinical picture accompanied by hematological disorders must raise awareness toward all MGRS components, and in cases, with low platelet count and hypocomplementemia ADAMTS 13 positivity strongly suggests the TMA. Kidney biopsy confirmation and treatment are vital for the kidneys even after ameliorating general clinical picture and laboratory parameters because in untreated cases, the kidneys will be further damaged. In contrast, treatment with complement inhibitors restores renal function and halts the progression to chronic kidney disease.

OP-14 Prevention of CKD in albanian population

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Introduction. Chronic kidney disease (CKD) is a progressive pathology with an increasing trend, which affects 5-15% of the population worldwide. Meanwhile the number of patients with RRT exceeds 2.5 million and it is thought to double in 2030.

Methods. This is a retrospective study, with descriptive and analytical character. The data came from medical files of patients who have received chronic hemodialysis (HD) during 2019 in the regional hospital of Gjirokastra. The estimated parameters are expressed with mean ± SD.

Results. The study population consisted of 46 chronic patients in hemodialysis. The average age was 60.9 years with a predominance of the group 61-80 years respectively 48%. Mostly they were men (63%) while women were only 37% of the total number. Patients' survival more than 14 years was only 7%. Arterial hypertension was observed in 65% of patients while 9% suffered from diabetes mellitus. The distribution of primary diagnoses leading to end stage renal disease was: 7 polycystic kidney disease, 4 nephrosclerosis, 3 IgA nephropathy, 1 pauci-immune vasculitis, 5 chronic glomerulonephritis without kidney biopsy, 12 chronic pyelonephritis, 3 diabetic nephropathy while 11 patients had no known primary diagnosis. The most commonly used vascular access was native arterio-venous fistula in 87% of patients while 6 patients received HD through veno-central catheter. But their first vascular access at

the start of HD had been a temporary CVC in 80% of the patients.

Conclusion. Prevention of CKD should have as a priority creating an information strategy of population around CKD and HD by organizing mini-discussion sessions at the workplaces and using the media and social applications to promote an active healthy lifestyle and the importance of check-up. Besides, the study shows the importance of performing the kidney biopsy by the nephrologist as a routine procedure.

OP-15 Liver steatosis predicts better CKD in MAFLD as compared to fibrosis by transient elastography with controlled attenuation parameter

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Introduction. Changing the term/concept of NAFLD to MAFLD enlarges the pathology with potential chronic renal involvement and possibly changes the epidemiology of CKD associated to liver disease. Our study explores the relationship between MAFLD and CKD using TE with CAP.

Methods. We evaluated 402 diabetic patients with MAFLD and high CKD risk using TE with CAP (FibroScan®). In order to determine the influence of fibrosis and steatosis severity on CKD prediction we used the cut-off values from a published multicentric trial compared with biopsy. CKD was defined according to KDIGO 2012 guidelines.

Results. The prevalence of CKD in our group was 60.8%. Patients with CKD had higher mean
LSM and CAP values than those without CKD. We found that hepatic steatosis is a better predictor of CKD risk compared to fibrosis. Univariate regression showed that CAP values> 353dB/m are predictive of CKD, and multivariate regression analysis, after adjustment according to sex, BMI, LDLc and HDLc, fasting glucose, showed that CAP values > 353 dB/m are more strongly associated with the presence of CKD compared to LSM (fibrosis) values.

Conclusion. In patients with MAFLD, CAP-assessed steatosis appears to be a better predictor of
CKD risk compared to LSM-assessed hepatic fibrosis.

OP-16 COVID-19 in kidney transplant patients-our experience

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Introduction. Kidney transplant patients have been identified as a risk category because of treatment with continuous immunosuppressive therapy. Our goal is to demonstrate the experience with COVID-19 in patients with a kidney transplant.

Methods. We studied 36 positive transplant patients (25 men), a mean age of 42 years who showed symptoms and have a positive PCR test. They were on continuous triple immunosuppressive therapy which included a steroid, mycophenolate mofetil, and a calcineurin inhibitor (cyclosporine or tacrolimus). The standard laboratory tests, including serum creatinine (SCr) from the last control, during and one month after recovery from COVID 19 were evaluated. Immunosuppressive therapy was modified or discontinued, apart from for the low steroid doses up to 15 mg. Positive chest X-ray and computed tomography were used to verify pneumonia. Further treatment was based on the recommendations for patients with COVID 19.

Results. The frequency of symptoms was: fever and fatigue (72%), loss of smell and taste (66%), muscle aches (58%), headache (36%), and diarrhea (19%). Twenty two patients needed hospitalization. Leukopenia was noted in 38%, enzyme abnormalities in 19%, high LDH in 47%, high d-dimers in 58%. 5 pts needed mechanical ventilation. Treatment included steroid therapy (27% methylprednisolone pulse) and covalent plasma in 6 patients. Significant increase in SCr before and during the disease 120 vs. 180 μmol/L ($n < 0.05$) and an increase in the percentage of proteinuria before and after healing 25 vs. 32%. The disease was fatal in 5 patients.

Conclusion. COVID 19 affects the function of the graft and has a high percentage of fatal outcomes. Adherence to preventive measures, vaccination, and early treatment is of paramount importance to this patients population.

OP-17 Different types of anca determine different clinical phenotypes and outcome in anca associated vasculitis (AAV)

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Introduction. Accumulating evidence supports the use of ANCA type to classify different clinical entities. We aimed to evaluate whether the presence and type of-ANCA determine different diseases, based on clinical phenotypes, renal involvement and response to treatment.
Methods. Differences in terms of clinical manifestations, disease activity, laboratory parameters and histology were recorded between patients with necrotizing glomerulonephritis (NGN) due to MPO-, PR3-ANCA (+) and ANCA (-) disease at time of diagnosis. Patients were treated with the same protocol, and followed up for 24 months, in a scheduled basis of every month for the first, and every 3 months for the second year. Primary end points were i) Combined end stage renal disease (ESRD) and/or death and ii) The presence of major or minor relapse during follow-up, and secondary end point was the combination of ESRD and reduction of eGFR ≥50%.
Results. Ninety-two patients (M/F 39/53, mean age 59.1±15years) diagnosed with NGN due to AAV, 36 (39.1%) PR3-ANCA, 39(42.4%) with MPO-ANCA and 17(18.5%) ANCA (-) were included. Number of involved systems differed significantly between PR3-, MPO-ANCA and ANCA (-), with only renal involvement in 3%, 25.5% and 29% of patients, 2 systems involved in 33%, 31%, 59%, and >3 systems in 64%, 43.5% and 12%, respectively, p=0.002. Histology classification revealed focal, crescentic, mixed and sclerotic type in 14%, 64%, 19%, 3% of PR3-ANCA (+), 8%, 28%, 18%, 46% of MPO-ANCA and 41%, 29%, 6% and 24% of ANCA (-), respectively, p50% e-GFR reduction in 8 (22.2%), 15(38.5%) and 5(29.4%) patients, respectively, p=NS, meaning that MPO-ANCA (+) patients showed a propensity to decline renal function. Rate of relapse was increased in the presence of PR3-ANCA (+), 14(38.9%), 4(11.8%) and 2(10.3%) of PR3-ANCA (+), MPO-ANCA (+) and ANCA (-) patients, had at least one relapse during the two years follow up p=0.006.
Conclusion. Clinical phenotype and renal histology differ significantly between PR3-ANCA (+), MPO-ANCA (+) and ANCA (-) disease and FNGN, however, renal function outcome is similar, despite the increased rate of relapses in PR3-ANCA (+) patients.

OP-18 Hemolytic uremic syndrome-western romanian evidence

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Introduction. Hemolytic uremic syndrome (HUS) represents a significant cause of acute kidney injury (AKI); 40% of the patients need an extrarenal supplementation method. Mortality decreased significantly (currently below 10%) with the improvement of renal replacement therapies.
Methods. We conducted a retrospective, observational study on all the cases of hospitalized HUS (typical and atypical) from the Children's Emergency Hospital "Louis Turcanu" from Timisoara, Romania. We included 12 cases of HUS from the last eight years, of which 9 cases of typical HUS and three atypical HUS.
Results. The age of the patients ranged from 8 months to 16 years (on average four years and three months) with a male: female ratio of 1:1,4, mainly from rural areas (66.6%). All patients with typical HUS had acute digestive symptoms with the identification of Shiga toxin in 44.4% of cases. 10 out of 12 patients required renal replacement therapy (1PD and 9 CVVHDF). Mortality was 16.6% (2 cases of typical HUS). From our group, seven patients resumed renal function (58.3%), and two patients (16.6%)-with atypical HUS- remained dependent on dialysis (1 HDI and 1 DP). Deaths were associated with severe neurological damage (stroke) in the first seven days after the onset of symptoms. Due to the need to initiate renal replacement therapy (83.33% of cases), the average length of hospitalization was increased (29 days).
Conclusions. 83.3% of patients required renal replacement therapy. Atypical HUS has progressed to end-stage renal disease depending on a form of dialysis (66.6%). Furthermore, mortality among children with HUS remains high.

OP-19 Efficacy and safety of Sinovac vaccine administrated in patients undergoing hemodialysis

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Introduction. In 2019, the number of Hemodialysis (HD) patients in Turkey was 61341.
This study aimed to evaluate the protection and safety of the COVID-19 vaccine produced by Sinovac by applying each of the two doses (inactivated) by looking at the Covid-19 antibody titers in undergoing HD patients.
Methods. Patients older than 18 years of age, undergoing hemodialysis treatment, and who had not had COVID-19 before were included in the study. 220 HD patients and 638 healthcare workers as control groups were included in this study. Before and 3±1 weeks after the vaccination, blood was taken from the patients, and their IgG antibody levels against SARS-CoV-2 were measured. Those with antibody titers above 50.0 AU/ml were considered positive and those below negative.
Results. Pre-vaccine antibody levels of the patients were studied. Pre-vaccine mean antibody level was 3.5±7.2 AU/ml and increased significantly three weeks post-vaccine antibody levels (mean 751±1196 AU/ml) in the HD group. Post vaccine mean antibody level was 1733±1888 AU/ml. The post-vaccine mean antibody level in controls was significantly higher than in HD patients (p<0.0001). Although it was higher in healthy controls, post-vaccination antibody response was accep-

table in both HD patients and control groups. However, the percentage of subjects with high antibody (>1000 AU/ml) levels was significantly lower in the HD group. Our patients did not had any allergic reactions or severe side effects related to the vaccine.

Conclusion. Antibody response Sinovac vaccine is produced in 85.2% HD patients group. However, the antibody titer is not as high as in healthy controls. Therefore, HD patients may need to follow for antibody titer, and further studies are required to define the clinical consequences of this low antibody titer.

OP-20 Risk factors for COVID-19 mortality in hemodialysis patients

Tomanoski V, Gjorgjievska G, Nakovska M, Krecova V, Kjamili G, Andonoski A, Ristoska K, Kachakova A, Zvezdakovska J, Kepeska S, Micajkova-Panova M, Ferati B, Veliu R, Tomanoska A, Zabzun Z, Kjamili M, Izairi S, Dauti H, Tancheva M, Trajkovska D, Jordanovska T, Stojanova E, Dimova K, Jagupi S, Veseli L, Stojanovski F, Jakupi G, Zekiri A, Dimitrioska A and Lozanoski D
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Introduction. The global pandemic with SARS-CoV-2 virus and Covid-19 threatened hemodialysis patients as a vulnerable category with a high risk for fatal outcomes. The study aimed to determine the prevalence and risk factors for mortality in hemodialysis (HD) patients with confirmed Covid-19.

Methods. This study was retrospective, multicentric, and included all HD patients with PCR test confirmed COVID-19 over ten months from March till December 2020.

Results. From total of 631 hemodialysis patients over 10 months, 162 patients (113 males and 49 females) or 25.67% were with positive PCR test for SARS-CoV-2. The mean age was 62.47±13.14 years and HD vintage 71.93±68.01 months. Over the observed period, 38 patients with Covid-19 (25 males and 13females) or 23.45% died. The mortality in patients aged 18-59 years was 15%, with 60-79 years 26%, and in patients with over 80 years was 50%. Clinical parameters showed that the deceased patients compared with survived patients had had statistically significant higher age (67.7±10.5 vs. 60.8±13.4 years; p=0.004), biochemical findings WBC ($9.1x10^9$/L±4.1 vs $6.4x10^9$/L±3.0; p<0.001), LDH (394U/L ±160 vs 294U/L±143; .p=0.032), D-dimers (3699ng/ml ±3568 vs 2025ng/ml±2628; p=0.041), lower s-albumin (25g/L±4.0 vs 34.6g/L±6.9; p<0.001), and less hospital days (9.8±12.1 vs 16.2±14.3; p=0.04). By logistic regression model, it was determined that the presence of chronic pulmonary disease (HR=6.18; p=0.008), ICU admission (HR=5.31; p=0.01), and malignancy (HR= 16.76; p=0.01) were the most predictive risk factors for mortality.

Conclusion. Our study showed that mortality is high in HD patients with Covid-19 and increases 23%, which is similar to other larger studies, like ERACODA and ERA-EDTA registry regarding mortality of hemodialysis patients with Covid-19 (25% vs. 20%). In HD patients significant association was found for increased mortality with the presence of chronic pulmonary disease, malignancy and ICU admission.

OP-21 Histological and immunophenotypical vessel changes in chronic kidney disease

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Introduction. Recent studies suggest the possibility of activating immune mechanisms in the onset and progression of atherosclerotic disease. The present study aimed to evaluate the role of immune mechanisms in the vessel of patients with Chronic Kidney Disease (CKD) and the association with clinical and laboratory indicators of atherosclerosis.

Methods. Patients with CKD stage V, in whom a radiocephalic arteriovenous fistula (RC-AVF) was created, were included in the study. Patients were divided in two groups, group A was consisted of patients who were on stage V, pre-dialysis, and being prepared to start on hemodialysis (HD), and those who had already been on HD for at least three years and were having a new RC-AVF formation, due to previous failure, group B. The control group included healthy volunteers who agreed to have a radial artery biopsy. The histological characteristics, inflammatory activation, and immunophenotypic alterations of the radial artery wall were estimated, and their association with the severity of calcification and atherosclerosis was studied. Also, the IMT was evaluated.

Results. Significant correlation was seen between inflammatory infiltration expression of CD3(+), CD20 (+), CD68(+) cells, cellular activation [CD34(+), a-SMA (+) cells], and calcification regulators (MPG, RANKL, OPG) with the degree of vascular calcification, and this was estimated and classified based on Verhoff's Elastic and von Kossa staining. The presence and severity of atherosclerotic lesions in CKD patients were assessed based on the measurement of common caro-

tid intima-media thickness (IMT) on both sides of the common and internal carotid.

Conclusions. Atherosclerotic disease in CKD appears to be directly related to inflammatory infiltration of blood vessels by T, B lymphocytes, macrophages, and myofibroblasts, as well as factors that affect calcification.

Poster presentations

PP-01 Chronic kidney disease in cancer patients, the analysis of a large oncology database from Eastern Europe

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Introduction. Kidney dysfunction is very prevalent in oncology patients and have an impact on their treatment and quality of life. The aim of our study was to analyze the prevalence of CKD in a large cohort of all-types cancer patients in a Western European Region.

Methods. We conducted an observational retrospective cohort study on 5831 consecutive, biopsy-diagnosed cancer patients between January 2019-December 2020 in the largest oncology hospital and outpatients clinic in Western Romania. In the statistical analysis 4342 subjects were included.

Results. From the 24 cancer types, the most prevalent cancers were represented by: breast (22.02%), lung (10.18%) and colonic cancer (9.51%). The prevalence of CKD (G3-G5) was 12.27% after the first year of follow-up and 13.42% in the second year. The prevalence of CKD was higher in patients with renal (50%), urinary tract (33.6%) and pancreatic cancers (19.6%) and lower in patients with colonic cancers (5.3%) and brain tumors (2.5%). At the end of our 2-year survey period, 0.7% of the cases had a eGFR around 6 ml – an indication for renal replacement therapy.

Conclusion. Oncology patients have a significantly higher prevalence of CKD compared to the general population, dependent of the age of the patients and the type of cancer. The prevalence of advanced CKD was surprisingly high (stages G4-G5PD 22.15%) one third of the CKD-G5 patients having indication for initiation of renal replacement therapy. An onco-nephrology team is a must for the best of medical care of these patients.

PP-02 Factors associated with anaemia in kidney transplant patients

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Introduction. Renal anemia is a common complication of chronic kidney disease (CKD). Anemia in kidney transplant patients has received relatively little attention in the literature, despite the high rate of recipients with anemia of 10-40% according to various studies. It is one of the most significant complications determining the quality of life of these patients. Our objective was to determine the risk factors for the development of anemia in kidney transplant patients.

Methods. The study included kidney transplant patients, a contingent of the Clinic of Nephrology and Transplantation. 590 patients aged 46.5±12.66, female/male ratio-1:1.3 were studied. Duration after kidney transplantation (KT) was from 3 month to 30 years. KT was performed from both deceased and living donor in a ratio of 1:1.8. All patients' data were from regular follow-up in 2018.

Results. Patients with anemia were n=94 (16%), of which with severe anemia (Hgb<60g/L) were n=4 (0.6%). Ratio m:f=1: 1.6. Mean age was 47.0±12.60 y. Average duration from transplantation 10±7.5 years. Significantly reduced glomerular filtration rate (eGFR=37.24 ml/min/1.73m^2±19.41) was found in patients with anemia, as well as significantly higher proteinuria - 0.81g/L±0.67. Lower hemoglobin values were found at higher eGFR in women than in men. Significantly higher percentages of m-TOR inhibitors, Azathioprine and Allopurinol in patients with anemia compared to the general population.

Conclusion. Factors associated with significant anemia in KT patients are: female gender, graft function, immunosuppressive and adjunctive drug therapy.

PP-03 C3 glomerulonephritis in post transplanted patient with MGRS (case report)

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Introduction. C3 Glomerulopathy includes several rare glomerulonephrites with underlying defects in the alternative pathway of the complement cascade. It is characterized by predominant C3 deposition in glomeruli due to abnormal activation of the complement system's alternative pathway. C3 GN has been reported to be associated with several systemic diseases.

Case report. We will describe a case presenting C3 GN in a patient with monoclonal gammopathy of renal significance (MGRS). A 61 years old man patient presented with gross hematuria, anemia, renal dysfunction (creatinemia 2.4 mg/dl), proteinuria 814 mg/24h. The patient had been transplanted two years ago, and was on corticosteroids, MMF, tacrolimus, and entecavir for hepatitis B. Serum protein electrophoresis showed: hypogammaglobulinemia with a small homogeneous spike-like peak. Serum kappa free light chains 32.4 mg/dl, serum lambda free light chains 9.3 mg/dl; ratio 3.4. Autoimmune tests ANA, ANCA, anti ds DNA, C3, and C4, were negative. Urine kappa light chains 26.4 mg/24h, urine lambda light chains 6.6 mg/24h. Urine kappa/lambda ratio 4. After consultation with hematologist results of bone marrow biopsy came for monoclonal gammopathy, and the FISH conclusion is the presence of t(11,14) (q13,q32), which originated from IgH/CCND1 retraction and 1q21 acquisition. Renal biopsy is C3 glomerulopathy with mesangial and diffuse endocapillary proliferation under light microscope and diffuse deposition of C3 and no immunoglobulin under an immunofluorescence microscope.
Conclusion. Monoclonal gammopathy of renal significance MGRS is a term to describe a group of hematological disorders associated with kidney disease that fail to meet the standard definitions for MM or lymphoma. In such cases, renal impairment is often linked to the underlying hematological disorder. The intention was to make a clear distinction between MGUS, a benign asymptomatic condition, and MGRS, which may be associated with significant morbidity and mortality.

PP-04 The first renal artery thrombosis treatment with percutaneous angioplasty in the Republic of Kosovo- a case report

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Introduction. Renal artery thrombosis (RAT) is a rare acute organ threatening condition. It can be successfully recognized in a healthcare system that provides multidisciplinary approach. Another challenge for the health care system is the disposal of advanced interventional treatment options. We present the first case of acute RAT treated with percutaneous angioplasty in the Republic of Kosovo, diagnosed in public and successfully treated in a private institution as result of integrated health system.
Case report. A 45-year-old male presented with a complaint of sudden onset of a right flank pain for 30 hours. Laboratory results reviled high serum creatinine and lactate dehydrogenase. The angiogram revealed the right renal artery with proximal occlusion. The thrombotic occlusion was traversed by using of a coronary guidewire to the distal portion but the branch arteries were extensively occluded with no parenchymal enhancement of the nearly total right kidney. After thrombus aspiration, bolus of GP IIb IIIa inhibitor was administered and good flow was obtained, but shortly after again diminished due to residual stenosis. So, drug eluting stent was deployed and the result was obtained. The patient's flank pain was entirely resolved after the intervention and the serum creatinine and LDH decreased to normal at fourth day. Also, hypercoagulable state work up was done, which was found to be positive for lupus anticoagulant and rheumatology consultation was recommended. The control angiogram reviled fully patent right renal artery, bilateral brachial artery occlusion, distal right femoral artery stenosis.
Conclusion. The renal artery thrombosis can be treated effectively by interventional angioplasty. It is a real health-care system challenge, especially in young developing countries.

PP-05 Avascular necrosis on both femur caused by systemic lupus erythematosus

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Introduction. Avascular necrosis (AVN), also known as aseptic necrosis or osteonecrosis, is bone death due to compromise of blood flow that leads to bone destruction, arthralgia, and loss of function in the joint. AVN remains a significant cause of morbidity in patients with systemic lupus erythematosus (SLE).
Case report. We report a 26 years old woman, diagnosed 7 years before with Lupus Nephritis. Initial presentations included: polyarthritis, malar rash, alopecia, oral ulcers, hypertension. Immunology laboratory tests indicate positive ANA and anti-ds DNA, with decreased complement levels, negative anticardiolipin, 24 h proteinuria 1.4 g/l proteinuria and microhematuria were detected in urinalysis. Based on all these facts and the criteria of American college of Rheumatology, the diagnosis of SLE complicated with lupus nephritis was done. A pulse therapy of methylprednisolone for 3 days was started, and very good results were achieved. In the following six years she was taking prednisolone. with bilateral constant hip pain, and worsened if she walked for a long distance and did not get better with analgesic. In evaluation with MRI she had bilateral osteonecrosis of femoral heads, Stenberg classification stage III. For period of 6 months noninvasive treatment was used, but with no success. Total hip replacement was performed 6 months, and now she came again to get 2nd operation total hip replacement.
Conclusion. Patients diagnosed with SLE are at high risk for AVN, especially femoral head. Use of steroids, and/or cytotoxic medication, were associated with this phenomenon. If the osteonecrosis is caught in an early

stage, the goal of therapy is to preserve the native joint for as long as possible. However, osteonecrosis often progresses, the mainstay of treatment is surgical using either a joint-preserving procedure, if possible, or total hip arthroplasty.

PP-06 Pain management in kidney transplantation

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Introduction. Appropriate pain management in kidney transplant recipients is required for optimal surgical results and graft survival. However, no agreement or guidelines for perioperative and postoperative pain management in kidney transplant recipients exist at this time. Therefore, we evaluated the perioperative and postoperative pain management practice in kidney transplant recipients in our country.

Methods. This observational clinical evaluation included all consecutive patients who underwent kidney transplant surgery. The primary measure of this evaluation was to access the current analgesia management practice. The VAS score, the need for 24 hours of analgesia, and the problems and/or adverse effects of pain treatment were additional measures in this evaluation.

Results. For the period of two years, thirty patients were enrolled in this evaluation. Two different types of pain management were mainly present among anesthesiologists. Epidural analgesia and total intravenous analgesia (17 vs. 13). The VAS pain score in the epidural group was lower at rest and on movement, but only for the first 2 hours (VAS at rest, 3 vs. 4), and on movement, 4 vs. 5. At the other evaluated time points, the pain score on the VAS scale did not differ between the groups. There was also a modest difference in side effects. Patients who received epidural analgesia experienced more adverse effects than those who received total intravenous analgesia.

Conclusion. Using a personalized pain management strategy will improve patient satisfaction and transplant survival.

PP-07 Which glomerular filtration rate is more reliable in adults with common variable immunodeficiency?

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Introduction. There are no comprehensive prospective studies examining renal complications in common variable immunodeficiency (CVID) patients. In this study, we compared creatinine-based estimated glomerular filtration rate (eGFR) calculation methods such as MDRD, CG and CKD-EPI with 24-hour urine creatinine clearance measurement to investigate which calculation method is more reliable and consistent in this patient group.

Methods. The records of 14 patients who had been clinically followed up at our clinic and were retrospectively reviewed. The eGFR values of the patients were measured by three different methods and compared with 24 h urine creatinine clarence.

Results. e-GFR calculated by the MDRD formula was 122.99±41.22 mL/min/1.73 m^2, while eGFR measured by 24-hour urinary creatinine clearance was 99.64 mL/min/1.73 m^2. In addition, eGFR calculated by the CKD-EPI formula was 113.83±26.46 mL/min/1.73 m^2, while eGFR calculated by the CG formula was 133.52± 45.35 mL/min/1.73 m^2. On average, there were differences of 23.9, 43.5, and 14.8 mL/min/1.73 m^2 in eGFR calculated by the MDRD, CG, and CKD-EPI formulas, respectively, when compared with the 24-h urine creatinine clearance (Figure 1). The correlation analysis between 24-hour urinary creatinine clearance and other formulas showed that 24-hour urinary creatinine clearance was positively correlated with MDRD, CKD-EPI and CG formulas (r= 0.726, p= 0.003; r= 0.634, p= 0.015; r= 0.806, p= 0.001; respectively).

Conclusion. We can conclude that the glomerular filtration rate calculated by 24-hour urinary creatinine clearance in patients with common variable immunodeficiency correlates with all three formulas, but the Cockcroft-Gault formula provides the closest result in terms of calculated mean eGFR.

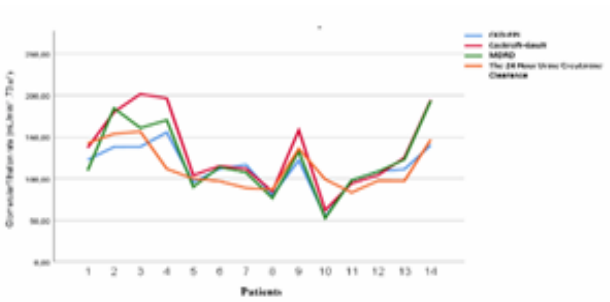

Fig. 1. Relationship between 24-hour urinary creatinine clearance and eGFR calculated by MDRD, CG, and CKD-EPI formulas

PP-08 Left ventricular structure and function in stable hemodialysis treated patients, a longitudinal multicenter cohort study

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Introduction. Left ventricular (LV) structure and function anomalies are frequent during the CKD continuum

and are associated with increased risk of mortality. Cross section and longitudinal ultrasound data are available for advanced CKD and transition to ESKD. Less information is available about LV changes during stable, long-term hemodialysis (HD) treatment.
Methods. All stable HD patients from 9 HD centers (1034 patients, 671 males, age 58.71±12.94 years) have been enrolled in January 2015. The cohort was followed-up for 4 years, kidney transplantation or death. Yearly, two-dimensional and M-mode continuous and Pulse Doppler echocardiography were performed.
Results. During the follow-up, the prevalence of cardiovascular comorbidities significantly increased (p< 0.0001), coronary artery disease (CAD) from 73.5% to 88.8%, peripheral artery disease (PAD) from 29% to 40.9%, cerebral vascular disease (CVD) from 20.4% to 30.8%, heart valves calcification (VC) from 65.6% to 89.3%, left ventricular hypertrophy (LVH) from 67.6% to 76.5%. The mortality risk increased with the presence of CAD (1.59-fold), PAD (1.61-fold), CVD (1.59-fold), and VC (1.77-fold). Mortality risk was increased in those with LVEF <50% (LVEF 40-49% 1.5 -fold and LVEF<40% 2.3fold). Among the survivors of the first year, LVEF varied (>5% decrease, >5% increase and +/-5% variations). More than 5% increase of LVEF was associated with higher mortality risk (crude 1.5-fold, adjusted 1.43-fold) compared to stationary EF (p=0.001).
Conclusion. Cardiovascular disease progresses during stable long-term HD therapy and increases mortality risk. HF becomes highly prevalent but only HF with decreased LVEF <50% is associated with increased risk of mortality.

PP-09 Acute kidney injury awareness in the paediatric population-a western romanian observational study
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Introduction. Acute kidney injury (AKI) represents an important cause of morbidity and mortality among the pediatric patients. To this day the incidence of AKI among hospitalized children is unknown. With this study we would like to draw attention on the AKI awareness and thus its clinical implications.
Methods. We conducted a retrospective, observational study on the hospitalized children between 2014 and 2020. The inclusion criterion was the diagnostic of AKI according to KDIGO 2012 definition.
Results. 127457 patients were hospitalized in the period 2014-2020 in Louis Turcanu Emergency Hospital for Children, Timisoara, Romania. The incidence of AKI was 1.46% (1867 cases). AKI aware was 27.48%. Mortality rate among AKI patients was 12.8% with the relative risk of death in the AKI aware group of 2.76. The odds ratio for death in the AKI aware group was 3,31.
Conclusion. AKI is a public health problem with major impact on the mortality in the pediatric population. The awareness of AKI is low (27.48%) with almost 3 times higher mortality rate.

PP-10 Covid experience in one dialysis center in North Macedonia-Diaverum (Vizbegovo)
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Introduction. Patients with ESKD undergoing hemodialysis therapy are vulnerable group with a high risk for developing an infectious disease because they are usually older and have multiple comorbidities. The purpose of this study is to determine the incidence and mortality of Covid-19 infection in patients visiting Center for Hemodialysis DIAVERUM Vizbegovo, the largest dialysis center in North Macedonia.
Methods. This is a retrospective analysis of all the patients treated in our dialysis unit in the period from 1.03.2020-1.10.2021. We analyzed all patients who tested positive for COVID-19 (PCR assay of the nasopharyngeal swab).
Results. In the study period 333 patient were treated in our unit. First positive detected case in our unit was on 09.06.2020 and further a total of 108 patients (32%) were confirmed positive. Reinfection has been demonstrated in three patients. Youngest patient was 17 years old, and the oldest 89 years old. The most common symptoms on presentation were fever and cough. Severe condition manifested in 50 patients (46%) and they were admitted to COVID hospitals, where 68 patients were with mild symptoms and were treated in our unit. Mortality was around 25,9% and was higher in female (57% vs 43%) and in older patients. The most common comorbidity was Hypertension (89%), followed by DM (43%), obesity (36%), AFF (25%), malignancy (25%).
Conclusion. SARS-CoV-2 has shown a high incidence and mortality rate in hemodialysis patients. The risk of mortality increases when patients require hospitalization. Age and other comorbidities like HTA are considered risk factors associated to worse prognosis in COVID-19. It is important to have high vaccination rate to reduce the need for hospitalization and mortality rate.

PP-11 Libman sachs endocarditis: as a cause of renal dysfunction in SLE
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Introduction. SLE, which causes any kind of kidney damage, can also cause damage with its cardiac effects, so it should be kept in mind.

Case report. Due to recurrent abortions, the patient diagnosed with SLE+Antiphospholipid antibody syndrome 8 years ago was referred from rheumatology for kidney biopsy. She had high creatinine levels and proteinuria. Blood test showed: SCr level 2.3mg/dl, WBC $7.9x10^9$, Hb 10.4gr/dl, PLT 192000, ANA negative; Anti dsDNA, APAs, direct Coombs test positive, C4 was low, ESR 85/h, spot urine protein/creatinine ratio was 4. There was no erythrocytes and no leukocytes found in urine. In the mean-time she had indication and was planned for mitral valve replacement. She had fatigue and shortness of breath. Echocardiography showed a nodular appearance in the mitral anterior and posterior leaflet, severe mitral insufficiency, and the valve tips were fibrocalcific. There was no growth in the blood cultures of the patient and no finding of lupus nephritis in the kidney biopsy. The patient underwent valve replacement surgery. There was no microbiological growth in the materials taken, and the material was also sent to pathology. The patient was discharged with serum creatinine level 1.4mg/dl and ESR 30/h after the operation.

Conclusion. SLE is a systemic disease, which can affect multiple organ function. In particular, it is very important to take a complete history from the patient and the perform the physical examination without skipping any steps.

PP-12 Comparison of arterial stiffness and serum biochemical and inflammatory markers in patients undergoing routine hemodialysis

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Introduction. In our study, it was aimed to compare arterial stiffness with various serum biochemical and inflammatory parameters and also to determine the possible relationships between arterial stiffness and end stage renal disease (ESRD) in patients with chronic hemodialysis.

Methods. 56 patients with ESRD who underwent routine hemodialysis 3 days a week were included. Age, gender, BMI, comorbid diseases, smoking habit, biochemical parameters and measured pulse wave velocity (PWV), augmentation index (Alx), central and peripheral systolic and diastolic blood pressures (SBP-DBP), peripheral pulse pressure (PPP) data were recorded.

Results. The PWV was detected statistically significant high in all these groups: DM, HT, PTH of below 150 pg/ml group than the PTH of over 300 pg/ml group, transferrin saturation 30-49% group than the transferrin saturation ≥ 50% group, albumin below 4 mg/dl group, CaxP of below 55 group (respectively p=0,026; p=0,04; p=0,04; p=0,017; p=0,003; p=0,004). No statistically significant correlation was found between PWV and ferritin, hemoglobin, LDL, central DBP and peripheral DBP (p=0.35; p=0.85; p=1,00; p=0.83; p=0.96). There was also a significant positive correlation between PWV and age, BMI, central DBP, peripheral DBP and PPP (p<0.001; p=0.025; p=0.025; p<0.001; p<0.001). Statistically significant negative correlation was found between PWV and CaxP, PTH (p=0.003; p=0.006). Alx was significantly higher in hypertensive group and CaxP≥55 group (p=0.021; p=0.026). Central SBP peripheral SBP and PPP were positively correlated with Alx (p=0.005; p<0.001; p<0.001). Gender, smoking and serum calcium levels were not associated with both pulse wave and Alx.

Conclusion. According to the data obtained from this study, many variables such as age, diabetes, hypertension, serum parathormone level, serum albumin level, central systolic pressure, peripheral systolic blood pressure, peripheral pulse pressure were effective on arterial stiffness in patients with routine hemodialysis.

PP-13 The effect of medication reminder in renal transplant patients

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Introduction. The aim of this study is evaluating the effects of using "medication reminders", one of the applications on mobile phones, which have been increasingly used in recent years, for kidney transplant patients. First 6-month period is the highest risk of rejection after kidney transplantation, frequency of rejection patients who use the "medicine reminder" application will be compared with those who don't. Supporting to use applications and questioning the usage in clinical controls can increase success of treatment. In this study, we investigated effect of "medication reminder" alarms/ applications, adherence to the treatment and kidney functions, in transplant patients who are multidrug users.

Methods. 85 patients who underwent kidney transplantation between Jan 2016-Sept 2020 were included. Patients were divided into two groups according to whether or not they or their relatives use "medication reminder" alarm/applications. Graft dysfunction and acute rejection were diagnosed by >30% decrease in eGFR or kidney biopsy. Modified Morisky Scale used for the research.

Results. Creatinine were statistically lower in app user patients at first and sixth months (first-month p=0.043 and sixth-month p=0.049) While the eGFR value was higher in the first month (p=0.044) in the app users, at the third-month (p=0.503) and sixth-month (p=0.051) no significant difference was observed. There was no significant difference in tacrolimus levels for both groups

at the first, third and sixth month (first-month p=0.085, third-month p=0.351, sixth-month p=0.457).
Conclusion. Most of the renal transplant patients use drugs other than the transplantation treatment, that could cause misusage. Hereby, we can reduce rejection by misusage of drugs.

PP-14 Hypothermia as concern in percutaneous nephrolythothomy

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Introduction. Hypothermia is a concern for surgical patients during the perioperative period. The aim of this evaluation is to assess the effects of two different irrigation solutions on body core temperature, shivering, visual analog scale score (VAS), and patient comfort.
Methods. Twenty patients with an ASA 1 and 2 score who underwent percutaneous nephrolithotomy (PCNL) under general anesthesia were enrolled in the study. The patients were randomly divided into two groups: the room temperature irrigation fluid group, group R, (n=10) and the warm irrigation fluid (37 ºC) group W, (n=10). Immediately after surgery and during the first postoperative hour, the patients' shivering, thermal comfort, VAS score, and body core temperature were monitored.
Results. All 10 patients in the R group developed hypothermia (body core temperature below 36 ºC). At recovery, the W group's VAS score was considerably lower than the R group's immediately after surgery (4 vs. 6), and in the first hour post-operatively (2 vs. 5). Shivering rates were found to be lower in the W group at 20% compared to 60% in the R group. Patients in group W had higher thermal comfort than patients in group R as well.
Conclusion. Using warm irrigation solutions for PCNL reduces hypothermia, postoperative pain score and shivering considerably. As a conclusion, a warm irrigation solution is recommended for this intervention. However, more research with a bigger sample size and multi center sampling is needed to achieve more definitive conclusions with more dependability and generalizability.

PP-15 Acute kidney injury in multisystem inflammatory syndrome in children associated with COVID -19

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Introduction. Multisystem inflammatory syndrome in children (MIS-C) is recently associated with Covid-19 infection. According to Centers for Disease Control and Prevention (CDC), MIS-C is characterized by persistent fever and laboratory markers of inflammation, multiorgan involvement and evidence of severe illness requiring hospitalization. Kidney involvement is also reported. We have analyzed data from our hospital of children diagnosed with MISC-C.
Methods. We conducted a retrospective study of children from 0-17 year old, hospitalized from November 2020 to September 2021 to University Children's Hospital, Skopje. Data are taken from patient records. All patient met criteria for MIS-C according to CDC guidelines. Renal function on admission and discharge was analyzed in all children. Children with acute kidney injury were categorized according to KDIGO criteria. Renal ultrasound and urine analysis were also analyzed.
Results. 31 children diagnosed with MIS-C were included. Acute kidney injury was present in 13% (4/31). Two of them were stage 3, one of them was stage 1 according to KDIGO criteria. The fourth child has chronic allograft nephropathy, her baseline serum increased 2.4 x baseline, categorized as stage 2. None of them required dialysis. Kidney function had good resolution in all of them, even in the child with kidney transplant serum creatinine returned to baseline values. Microscopic hematuria was present in 16% (5/31). In all children with AKI renal ultrasound was normal. 80% of children (25/31) were treated with corticosteroids and intravenous immunoglobulin.
Conclusion. In our cohort of children with MIS-C renal injury matches with reports from other centers (10-46%). Kidney function in all children had good resolution. Because the pathophysiology of kidney injury in MISC-C is not yet established, these patients need long-term follow-up.

PP-16 Recurrent hyperparathyroidism after subtotal parathyroidectomy in a patient with chronic kidney disease. A case report

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Introduction. Parathyroidectomy (PTX) is considered the best treatment of primary hyperparathyroidism (PHPT) for symptomatic disease or patients with organ damage such as presence of renal stones. Many studies have demonstrated the benefit of PTX in decreasing the progression of chronic kidney disease (CKD) and the benefits in long-term outcomes. We report here a case of recurrent hyperparathyroidism in a patient with persistent renal dysfunction, demonstrating the difficult dilemmas that can rise for the treatment.
Case report. A 49 years old male with a past history of PTX for parathyroid adenoma before 15 years, was admitted to our unit due to labile level of blood pressure, fatigue and weakness. Laboratory examinations revealed an increased serum creatinine to 4.04 mg/d in a patients referred as with stable renal function during the last year, with eGFR between 50-55 ml/min/1.73m².

The patient had increased level of Calcemia (10.8 mg/dl), with normal serum phosphate level. The level of PTH was increased to 400.3pg/ml compared to 62 pg/ml from the last evaluation. Renal ultrasound showed a reduced echogenicity of the cortex but no evidence of kidney stones. Parathyroid scintigraphy using Tc-99m sestamibi (20mCi) showed a higher tracer uptake in the inferior parathyroid sinister gland. According to these data the diagnosis of a recurrent PHPT was made in a patient with renal deterioration function probably related to duration of hypercalcemia. The decision was made to propose subtotal PTX. After the surgery, serum calcium was in normal value and PTH 48pg/ml. Although, three months after intervention serum creatinine levels remained high, 2.8 mg/dl but significantly reduced compare to before surgical treatment.

Conclusion. We present a rare case of recurrent hyperparathyroidism in a patient with a history of previous parathyroidectomy for parathyroid adenoma. In fact, this case highlights the difficult choice of surgical intervention in a patient with coexisting renal dysfunction. Therefore, the potential benefit of parathyroidectomy should be weighed against the possible major risks of intervention.

PP-17 Pregnancy and chronic kidney disease: a case report

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Introduction. Pregnancies in women with chronic kidney disease are always a challenge that require integrated multidisciplinary care. The obstetric outcome in women with kidney disease has been improved lately due to continuous progress in medical management of hypertension and renal disease.

Case repost. We present a case of a patient with chronic renal disease admitted to the obstetrical first aid department at the 35th week of pregnancy with headache, legs edema and hypertension. Her medical history included four pregnancies (two live births and two miscarriages). According to the patient's history, she developed hypertension early at 20 weeks of pregnancy. Previously the patient was diagnosed with left kidney atrophy and chronic renal failure with serum creatinine at 1.9 mg/dl and proteinuria on dipstick (660 mg/dL). When the woman was admitted to the obstetrical department, she had high blood pressure (175/90 mmHg) and diffuse leg edema. The patient developed nephrotic range proteinuria and signs of progressive decline of renal functional. Laboratory workup revealed total serum protein (5.7 gr/dL), a reduction in serum albumin (2.3 mg/dL), and an increase in uric acid (7.9 mg/dL), serum creatinine (3.6 mg/dL) and hemoglobin levels at 9.7 mg/dL. Cesarean section was performed two days after admission. Both mother and premature baby (1600 g) were in good and stable conditions. The patient was discharged after 6 days, her blood pressure was normal under treatment, 24-hour proteinuria reached progressively pre-pregnancy levels and serum creatinine was 3.2mg/dl.

Conclusion. Pregnancy always remains an open challenge to nephrologists. The association of pregnancy and renal failure at any degree caries a higher risk of fetal and maternal complications. The prognosis often depends on the values of serum creatinine prior to pregnancy, the degree of worsening of renal function, development of preeclampsia, nephrotic syndrome and intrauterine gestational restriction.

PP-18 A successful endovascular intervention of Nutcracker syndrome for the first time in Albania: case report

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Introduction. Nutcracker Syndrome (NS) is a rare vascular disorder. This condition is caused by left renal vein (LRV) compression between aorta and superior mesenteric artery (SMA). Nutcracker Syndrome can cause hematuria, flank pain and in some cases orthostatic proteinuria.

Case Report. A 23-year-old woman was presented with intense left lumbar and pelvic pain in the emergency department (ED). The patient denied other symptoms like fever, dysuria, diarrhea/constipation. She refers that in the past few months she had been going to the ED because of this progressive abdominal pain and hematuria. A general workup was done such as complete blood cell count, renal and liver function tests which were in a normal range. However, the urinalysis showed traces of microscopic hematuria. Performed abdominal ultrasound, computed tomography and angiography that showed proximal dilatation of the LRV and inverted flow in varicose gonadal vein with important collaterals. By these findings the diagnosis of Nutcracker Syndrome was done. The patient underwent an endovascular stenting procedure, 14mmx40mm self-expanding Wallstent was implanted in the renal vein. After the procedure flank pain resolved and postoperative computed tomography with i.v. contrast showed that the stent was in a normal position.

Conclusion. Hematuria is a common urinary abnormality in kidney diseases. Nutcracker Syndrome is a rare disease that is why a high suspicion is required to detect it, not only to the relieve symptoms but more importantly to prevent chronic damage of the kidney. We reported a NS and successfully endovascular treated it with renal stenting, for the first time in Albania.

PP-19 Desensitization to rituximab of a patient with membranous nephropathy and rituximab allergy

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Introduction. Rituximab is a monoclonal antibody, recently recommended as first choice in treatment of membranous nephropathy. Among biological agents, rituximab has the highest reported reactions during infusions. Rapid desensitization is a procedure that allows for the safe readministration of a drug after a previous hypersensitivity reaction. We aim to describe our experience with rapid desensitization to rituximab in a membranous nephropathy patient with rituximab hypersensitivity.
Case report. We present a case of a 48-year-old male patient with weight gain, lower extremity edema, arterial hypertension, and nephrotic range proteinuria. The patient was diagnosed with membranous nephropathy 14 years ago with relapses and remission of disease, despite different treatment over the years. Last year, the patient was recommended to start the treatment with rituximab. Two separated doses of 1g rituximab were administered during February 2020 with a total remission for the next 15 months. The disease relapsed, probable due to COVID infection and nephrologists decided for another treatment with rituximab. During the drug administration, the patient developed flushing and dyspneal 30 min from the start. This was defined as Grade 2 reaction according to the Brown Classification, which indicates a moderate systemic hypersensitivity reaction. Skin testing was performed 4 weeks after the reaction. Prick test with rituximab 10mg/mL and intradermal test with 1:100 to 1:1 dilution of the drug resulted negative. Because the sensitivity of skin testing with mAbs is not known, we planned a 12-step rapid drug desensitization protocol which resulted succesful for our patient.
Conclusion. Rapid desensitization with Rituximab is a helpful method for drug readministration after a hypersensitivity reaction, in cases in which there are no reasonable therapeutic alternatives.

PP-20 Clinical outcomes of hospitalized COVID-19 patients with kidney disease: a single center observational study from specialized hospital of nephrology

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Introduction. COVID-19 caused by SARS-CoV-2 becomes a global pandemic. Chronic kidney disease, end-stage renal disease (ESRD) patients on maintenance hemodialysis, and transplant patients are all specific and highly vulnerable to infections. This study aimed to provide evidence on COVID-19 incidence, characteristics, and mortality in CKD patients followed up in an integrated healthcare program in our hospital. The study population included CKD, CKD on MHD, and transplanted patients recruited in the Institute of Nephrology in Struga from March 2020-2021.
Methods. We present an observational study of clinical outcome of hospitalized COVD19 patients with CKD and MHD in our hospital during one year, March 2020 till March 2021, 82 in total, 31females. Data were retrospectively analyzed from our department of dialysis database.
Results. Fifty-eight had chronic kidney disease on MHD, twenty-two were CKD (stage II-IV), and two were transplanted patients. The mortality rate was 28.2 %. Ten patients were treated conservatively with no need for HD treatment. Twelve patients started treatment with hemodialysis for the first time, three of them were discontinued from HD, five were maintained on hemodialysis treatment after recovery of SARS-CoV-2 infection, and four patients passed away. Fifty-eight patients had a clinical presentation with bronchopneumonia, but the other nineteen had no pulmonary involvement. Five patients due to clinical presentation were sent to the tertiary level. It is essential to mention that seven patients had advanced stages of malignancies of various etiologies.
Conclusion. The incidence of COVID-19 among these patients was strongly related to the spread of the infection in the community, while its lethality is associated with the underlying kidney condition and comorbidities like diabetes and arterial hypertension. COVID-19 related mortality was about ten times higher than that of CKD patients without COVID. For this reason, it is urgent to offer direct protection to CKD patients by prioritizing their vaccination.

PP-21 Severe hypertension in a young man with aortic coarctation

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Introduction. Aortic coarctation is a common cardiac congenital defect. This defect affect mostly males. The classic coarctation of the aorta is located in the thoracic aorta, distal to the origin of the left subclavian artery. Aortic coarctation is found in 6-8% of all cardiac defect. Its clinical sign is hypertension. In auscultation of this patients a sistolic interascapular murmur can be heard. Usually this pathology is diagnosed in early childhood.
Case report. We present a case of 24 years old man suffering from headache, vertigo and very high blood pressure until 220/110 mmHg during the last month. The patient referred that he did not suffer from any known pathology before. The laboratory findings were normal. In echocardiography examination, suprasternal view we sow stenosis of aorta with gradient 84.6 mmHg; V max 4.6 m/s. The aortic stenosis (aortic coartation) was then confirmed in computed tomography angiography: 3 cm distal left subclavian artery the aorta was stenotic till 6 mm. The patient underwent percutaneous stent implantation for aortic coarctation. Three months later the patient was found normotensive.

Conclusion. Aortic coarctation should be suspected even in a young adult patients with hypertension. Every patient with hypertension, systolic interscapular murmur, cardiac insufficiency signs (at late stage) must underwent echocardiography examination. Early diagnosis is responsible for long term survival of these patients.

PP-22 Elderly patients with acute kidney injury- the effect of treatment on short- term outcomes

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Introduction. Acute kidney injury (AKI) is characterized by an abrupt decline in renal function occurred within hours or days. The incidence of AKI in elderly population (≥ 65) is up to 10 times higher compared to patients under 65 years of age, with an increased requirement for dialysis treatment. Older patients with AKI have an elevated risk of both short-term and long-term mortality.

Methods. 70 elderly AKI patients who were admitted in University Clinic of Nephrology, Skopje, were enrolled in the study, prospectively, during the 8 months period. All included patients had a hospitalization over the 24 hours and filled one of the criteria of AKI definition. According to outcome and treatment, patients were divided into two groups.

Results. The median age of this population was 74.28± 6.64 years, (53% female), with mean CCI (Charlson Comorbidity Index) score of 6.94±1.94. The most common comorbid conditions were chronic heart failure, with 47% of patients and diabetes mellitus, with 42.8%. Pre-existing chronic kidney disease was present in 44.3 %. The majority of patients (70%) were classified at stage 3 of AKIN, 20% of patients were classified at stage 2 and 10% at stage 1. The group of survivors had significantly higher diuresis (p=0.001) and also a longer hospital stay (p=0.000). In the groups of patients with death outcome, the chronic cardiomyopathy was more frequently present (p=0.034). In terms of treatment, 58.6% of the AKI patients underwent hemodialysis while 41.4% received conservative treatment. Mortality rate was 52.8%, out of which 28.6% was in-hospital mortality, while in 24.3% of patient death occurred in follow up period up to 90 days.

Conclusion. High comorbidity burden is common in elderly patients who are at higher risk for the development of AKI. In our study survival is not related to different treatment options, but decreased urine volume is associated with lower survival. Applied treatment in elderly patients with AKI should be assessed by measuring the long term outcome.

PP-23 Characteristics and prognostic factors for outcome in elderly pateints with acute kidney injury

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Introduction. An association between AKI and the elderly has long been recognized. The elderly are particularly vulnerable for renal insults and the incidence rate of acute kidney injury is highest in this population. Coexisting disease that occur during the aging process increase the risk of AKI in elderly population. This study aimed to investigate the clinical characteristics and prognostic factors for outcome in the elderly patients with AKI and help improve prognosis.

Methods. 101 elderly patients (≥ 65years) who filled out one of the criteria of definition of AKI according to KDIGO, were included in the study. Patients were divided into 2 groups by age, group <75 and group > 75 years old. The burden of the simultaneous presence of comorbid conditions was estimated through the Charles Comorbid Index (CHI). In terms of outcome they were divided in group with short and 90-day survival.

Results. The mortality rate for the 90-day follow-up period after the AKI event was 45.5%. The intra-hospital mortality rate was 22.8%. In our study the age was not a risk factor for intra-hospital and 3-month outcome of patients with AKI. The presence of comorbid conditions, was not significant between survivors and deceased patients with AKI (p=0.39, p=0.28 consecutive). Cox regression analysis confirmed the CCI score as a significant factor of survival in patients with ABO, (p=0.036).The risk of mortality increased by 16.3% with each increase in this unit score. Cox regression analysis confirmed heart diseases as a significant prognostic factor for survival, increasing the risk of fatal outcome by about 2 times. We found a significant difference in survival time, depending on the presence of heart disease as a comorbidity (p=0.037). Conducted Cox regression analysis showed that HR-for heart disease, as a comorbidity, is 1.83 (1.020-3.306) and p= 0.043. Cumulative survival was higher in the group of patients without cardiomyopathy-64.2% (0.07) compared to the group of patients with cardiomyopathy-43.8% (0.07).

Conclusion. AKI survivors with high burden of comorbidities are at high risk for post discharge death. Cardiomyopathy, as a risk factor, for two times increases the risk of death. CCI score is significant independent high-risk prognostic factors for poor outcome in elderly patients with AKI. Remain the recommendation for individual clinical approach, assessment and selection for the application of treatment taking into account the overall condition in adult patients with acute renal injury.

PP-24 Secondary Antiphospholipid syndrome at a young male

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Introduction. Antiphospholipid syndrome (APS) is an autoimmune disease characterized by the occurrence of venous and/or arterial thrombosis, and the detection of circulating antiphospholipid antibodies. APS occurs as a primary condition, or secondary (it can occur in the presence of systemic lupus erythematosus (SLE) or another systemic autoimmune disease). The diagnosis APS is based on a combination of clinical features and the presence of one or more of the following antiphospholipid antibodies (LAC, aCL antibody or aβ2GPI antibody present on two or more occasions, at least 12 weeks a part). A clinically significant aPL profile has been detected in approximately 30% of patients with SLE.

Case report. We are describing a rare case of a 23 years old male who was presented with dyspnea, retrosternal discomfort, fatigue, general weakness, joints pain over a period of 3 months. One single episode of syncope was his first clinical symptom 3 months ago which continued with the clinical manifestation as mentioned above. He was at first diagnosed as Thrombocytopenia in 2007 and Systemic Lupus Erythematosus (SLE) in 2020. When the patient was hospitalized at our clinic, he referred headache, dizziness and elevated blood pressure (170/100 mmHg). Moreover, laboratory and imaging examinations showed bilateral pulmonary thromboembolism and positive Anticardiolipin antibodies, positive ANA, positive SSA & SSB.

Conclusion. It can be very difficult to diagnose an APS at the beginning in the absence of classical symptoms. Though APS is one of the most common thrombocytophilias, unfortunately, it is not recognized often enough. Clinicians should investigate for the presence of antiphospholipid antibodies, as early diagnosis may influence the course of the disease.

PP-25 A rare case of a young female with seronegative-catastrophic Antiphospholipid syndrome

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Introduction. Catastrophic antiphospholipid syndrome (CAPS) is a rare but potentially life-threatening condition characterized by diffuse vascular thrombosis, leading to multiple organ failure developing over a short period of time in the presence of positive antiphospholipid antibodies (aPL). CAPS is a severe form of antiphospholipid syndrome, developing in about 1% of cases of classic antiphospholipid syndrome, manifesting as microangiopathy, affecting small vessels of multiple organs.

Case report. We are describing a rare case of a 33-year old woman who was presented to the internal medicine clinic with 10-day history of intense abdominal and right flank pain, nausea, vomiting, joint pain, shortness of breath, severe headache and one episode with loss of consciousness. She was at first diagnosed as Partial Seizure of Vascular Origin (2010); Seronegative Arthritis (2012) in treatment with Valproic Acid and Aspirin 100 mg/day; Prednison 5 mg/day (interrupted in the past 3 months). Her medical history was notable of three miscarriages. Laboratory and imaging examinations showed bilateral pulmonary effusion, left apical pulmonary consolidation, minimal pericardial effusion, total thrombosis right kidney, partial thrombosis left kidney, multiple spleen thrombosis, multiple gliotic lesions in periventricular white matter and negative aPL, positive ANA, anti-ds DNA, anti-RO, anti-RNP, anti-La, with renal and hepatic impairment. Based on the patient's medical history (syncope, 3 pregnancy losses) and on CAPS's Criteria: Renal Infarction, Spleen Infarction, Multiple Gliotic Lesions, was diagnosed with Seronegative CAPS.

Conclusion. CAPS is a systemic autoimmune disease, the most severe form of APS. The diagnosis can be challenging, especially in patients with negative antiphospholipid antibody. Early diagnosis and prompt treatment play a crucial role to save the patient's life.

PP-26 Can the serum creatine kinase (CK) level be a malnutrition parameter in patients with end-stage kidney failure?

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Introduction. The aim of this study was to investigate the relationship between serum CK levels and malnutrition parameters in patients undergoing hemodialysis (HD) and peritoneal dialysis (PD) for end stage renal disease (ESRD).

Methods. In this prospective study, 60 patients receiving HD and 30 patients receiving PD for ESRD were evaluated. The laboratory findings specific to malnutrition measured in the last 3 months synchronously with CK were reached through the hospital information system, thanks to the routine followups of the HD and PD patients, in order to assess the laboratory data for the nutritional condition of the patients. The relationship between serum CK levels and Mini Nutritional Assessment (MNA) Test scores, albumin, C-Reactive Protein (CRP), arterial blood gas parameters, KT/V ratio, total body water, muscle mass, body mass index (BMI) and lean body mass (determined by Bioelectrical Impedance Analysis (BIA) were examined.

Results. No correlation was found between CK levels and age, dialysis duration and Ca serum values in HD and PD patients (p>0.05). A positive correlation was found between CK levels and MNA scores and triceps skinfold thickness, lean body mass, body muscle mass and BMI values of PD and HD patients, and a significant negative correlation between total body water values (p <0.001).

Conclusion. In the present study, it was revealed that serum CK level was correlated with the parameters in BIA method that has been increasingly used recently, which is compatible with the literature. MNA test is a method widely used in determination of malnutrition and it is recommended in determination and follow-up of malnutrition by international guidelines. A statistically significant correlation was determined between serum CK levels and MNA scores both in HD and PD patients (p <0.001).

PP-27 Vascular access as a key point for a good adequacy of dialysis

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Introduction. Vascular accesses consist of permanent arteriovenous (AV) accesses (autogenous fistulas and synthetic grafts), tunneled venous catheters and temporary central venous catheters (CVCs). AV accesses have fewer complications than venous accesses, and are therefore the preferred hemodialysis access. An important additional issue is whether the type of access influences adequacy of dialysis (i.e. Kt/V). Key limiting factors in delivering adequate Kt/V are blood pump speed (QB), access recirculation, and treatment time. The aim of our study was to compare dialysis adequacy between patients with AVF and those with CVC on three different aspects: comparison of dialysis efficiency, comparison of nutritional status and the extent of anemia between these two groups of patients.

Methods. All patients were dialyzed with identical machines. Our study included 48 patients who were regularly treated with bicarbonate hemodialysis. All patients were dialyzed through AVF or CVC.

Results. 27 patients had AVF for vascular access, 21 males and 6 females, with the median age of 66 years. On the other side, 21patients were dialyzed through CVC, 13 males and 8 females, the median age was 59 years. 96% of patients with FAV achieved Kt/V dialysis adequacy >1.2 and 66.6% of them had Hb>10 gr/dl, while in group patients with CVC, 57% of them achieved adequacy of dialysis Kt/V>1.2 and 57% of them had Hgb>10 gr/dl.

Conclusion. AV accesses are superior to venous accesses because they are less prone to complications and are more likely to deliver prescribed Kt/V within prescribed treatment time.

PP-28 Perception of kidney disease amongst general population

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Introduction. While prevalence of CKD is globally increasing, nationwide incidence has reached approximately 130 per million. Resembling regional and European trends, diabetes and hypertension are increasingly pointed out as the most prevalent causes. Awareness about kidney disease potentially has an important impact on prevention, diagnosing, and treatment. Aim of the study was evaluation of the perception and knowledge of our population about kidney disease.

Methods. Study included subjects from urban and rural areas, without known renal disease, diabetes or hypertension. A simple questionnaire consisting of 5 general and 8 specific questions was applied.

Results. The study included 922 subjects with mean age 44±18 years old, of which 57.1% female, 86,6% living in urban areas, 54,4% with university education, 9,6% unemployed. 20.6 % had a recognized person diagnosed with a kidney disease, 12.9% never had a spot urine test. The link between diabetes and kidney disease was acknowledged by 52.8%, while 29.2% denied that link and 18% had no information. Interestingly 75.7% of subjects acknowledged a link between hypertension and kidney disease, but the reciprocal causative association was confirmed only by 47.2% of subjects in this group. Most cited renal diseases were kidney stones (40.2%) and urinary infections (36.2%). 13.6% of subjects responded completely right. The knowledge was significantly better in subjects who had a recognized person with kidney disease (p=0,01) and in urban group (p=0.038). We found no significant difference of knowledge according to education, gender, age or employment status.

Conclusion. Our population needs education about kidney disease, focusing on link with diabetes and hypertension and far beyond kidney stones or simple urinary infections.

PP-29 A good nutritional state in dialysis might overcome the effect of inflammation on atherosclerosis

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Introduction. Dialysis patients are highly prone to atherosclerosis. We evaluated patients on PD and MHD treatment, for the presence of atherosclerosis and its link with inflammation and nutritional status.

Methods. In a cross-sectional study, 102 patients on dialysis treatment for ≥3 months, of which 47 patients on PD, were evaluated for the presence of atherosclerosis using carotid arteries B-mode ultrasonography. The athe-

rosclerosis was confirmed in case of CIMT >10mm and/or presence of plaque. Inflammation was evaluated using CRP (mean value of the last 6 months). Nutritional status was evaluated with 7 points SGA score.
Results. Atherosclerosis was found in 64.7 % of patients and inflammation was present in 39.2%. Although inflammation was significantly more pronounced in PD (57.4%) than HD patients (23.6%) (p=0.002), there was no difference in atherosclerosis presence in PD versus MHD patients (respectively 63.8% vs 65.5%, p=0.28). We found a better nutritional status in PD group and non-atherosclerotic group, with evidence of a signifycantly higher SGA score in those two groups, compared respectively to MHD ($p<0.05$) and atherosclerosis group (p=0.035). After multivariate regression analysis SGA score was found independently and significantly associated with atherosclerosis (OR 1.86) as was CRP, age, diabetes, PTH and phosphate.
Conclusion. A low SGA score is associated with atherosclerosis in dialysis patients. Keeping a well-nourished status might out-weight the effect of inflammation on atherosclerosis.

PP-30 Glioblastoma in kidney transplant recipients: case report

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Introduction. Intracranial glioblastoma after a kidney transplant is a rare complication. The use of immunosuppressive therapy to preserve the allograft function can significantly increase the incidence of malignancies in transplanted recipients compared to general population. Cases of glioma are less frequent described. The ability to identify and prevent solid organ tumors in the transplanted patient, depends on regular screening examinations and strict adherence to prophylactic measures. Screening the patient and donor prior to transplant can help to detect any underlying pre-existing malignancy.
Case report. A 56 years old female, with history of end stage renal disease due to chronic pyelonephritis, treated 4 years with hemodialysis, underwent kidney transplantation in 2018. The kidney donor was her husband 61 years old. She was maintained on three immunosuppressant drugs: prednisolone, *mycophenolate mofetil* (MMF) and tacrolimus. Laboratory results: WBC 6.7 $x10^9$, RBC $4.5x10^{12}$, Hb 12.8 g/dl, BUN 26 mg/dl, creatinine 0.9 g/dl, blood level of tacrolimus 5.3 ng/ml, TSH 0.6 UI/ml, HIV negative. Three years after transplantation the patient was presented to the clinic with headache, trembling face, loss of consciousness for 10-15 seconds, without muscle contractions. Based on MRI the diagnosis of intracranial glioblastoma was confirmed. Patient was treated with radiotherapy for 5 weeks and continues the treatment with Levetiracetam.
Conclusion. Kidney transplant recipients are at higher risk of developing carcinoma. Epithelial cell neoplasia has been described in 50% of cases. The most common neoplasm involving the CNS of transplant recipients is non-Hodgkin lymphoma while glial tumors are rarely described. Several hypotheses have been proposed to explain a possible link. One possible factor may be the immunosuppressive state of recipients as a result of post-transplant administration of immunosuppressive drugs, as it is known that gliomas have an higher incidence in HIV-infected patients. However, it is not yet clear whether immunosuppressive drugs acts as a direct transforming factor.

PP-31 Silent brain infarctions in hemodialysis patients

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Introduction. End Stage Renal Disease (ESRD) is associated with an increases risk of cerebrovascular accidents with significant morbidity and mortality. Stroke is the third most common cause of cardiovascular disease death in hemodialysis patients. Chronic renal disease is an independent risk factor for stroke in the general population. The aim was to highlight the risk factors for stroke in our dialysis population, to see the prevalence of stroke in this population and to find evidence of "silent infarcts".
Methods. We conducted a retrospective, qualitative and descriptive study which involved 1732 patients from 5 different centers in the Amerikan Hospital from November 2008 to December 2019. We identified 70 different case of cerebrovascular accidents. Also we had a control group of 70 dialysis patients to compare, (those we did not select it preferentially but we selected according to the ordinal registrations in to the centers).
Results. A total number of 1732 patients were observed during November 2008 till December 2019. Of these 70 patients were diagnosed with cerebrovascular accidents. The mean age was 57.6 years. 33patients were females (47%) and 37 patients were males (53%). 23 patients were younger than 55 years old and 47 patients (68%) were older than 55 years. The mean age of the control group is 53.69 years. The vascular access in 22 patients was AVF (fistula 30.4 %) and 48 had a central venous catheter (69.6%). In the control group there were 52 AVF (74.3%), 1 GAV, and 17 CVC (24.3%). The average hemoglobin levels in the stroke group was 9.3 g/dl compared to 11.4 g/dl of the control group.
Conclusion. The prevalence of stroke among hemodialysis patients in our center resulted 4.01%. The patients with stroke tended to be older, with lower hemoglobin values and the central venous catheter represented the vascular access in the majority of the patients (69.6%). Vascular access may increase stroke risk by affecting cerebral hemodynamics.

PP-32 Factors associated with increased risk of hospitalization among patients with diabetic kidney disease

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Introduction. The prevalence of diabetes in Albania has increased rapidly in recent years and is likely to continue to increase in the future, with important implications for health policy. Our local data revealed that 18% of patients undergoing dialysis in Albania have diabetic nephropathy as a cause of renal failure. The aim of the study was to assess the excess of morbidity and factors associated with hospitalization for patients with diabetic kidney disease.

Methods. This is a single center study of patients with diabetic kidney disease attending nephrology service during 15 months. We evaluated the cause of hospitalization and analyzed the risk factors. Multivariable regression was used to identify factors associated with hospitalization rates.

Results. 102 patients were included in the study, (57% males and 43% females), with a mean age 60.4±15.8 years. The mean duration of diabetes was 9.3±5.9 years. 14.3% of patients had a blood pressure <130/80 mmHg. Only 19.5% of patients on stage 3 and 4 of CKD were not taking either an ARB or ACE inhibitor. HbA1c levels and fasting plasma glucose levels were significantly higher in diabetics with macroproteinuria ($p<0.001$). We found that all-cause hospitalizations were associated with older age, (≥62 versus 45 to 61 years), more proteinuria (≥500 versus <300 mg/g), higher systolic blood pressure (≥140 versus 120 to <130 mmHg), higher HbA1c levels, and lower eGFR. The most common causes of hospitalization were related to metabolic (41.8%), cardiovascular (29.8%), infections (11.7%), respiratory (6.7%) causes and macroproteinuria (10.8%). We found that the rates of cardiovascular hospitalizations were higher among those with ≥500 mg/g of proteinuria irrespective of eGFR.

Conclusion. We observed a high rate of hospitalization for patients with DKD even for those with moderate reduction in kidney function. We found that high levels of proteinuria and reduced cardiac function have the largest association with hospitalizations across a wide range of kidney function levels. Together these findings support the need to increase the opportunities for early interventions and effective follow up of patients.

PP-33 A rare nephrotic syndrome case with hypotension and rapid mortality: primer amyloidosis

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Introduction. Although renal involvement is often in the form of asymptomatic proteinuria in patients with AL amyloidosis, clinically it can be seen a wide ranges from overt nephrotic syndrome. If the primary and secondary nephrotic syndrome etiologies are viewed, its hypotensive course distinguishes AL amyloidosis from other causes.

Case report. 61-year-old female patient was referred from the pulmonology clinic to the nephrology clinic because of oliguria. The chief complaints were fatigue, decreased urine output and shortness of breath. After the patient was diagnosed with congestive heart failure 2 months ago, bilateral massive pleural effusion developed and a right tube thoracostomy was placed. Apart from this, the patient had been operated on 2 years ago for carpal tunnel syndrome. Arterial blood pressure was 80/50 mm/Hg, heart rate was 50 beats/min. Biochemical parameters: sodium 129 mmol/l, potassium 5.68 mmol/l, phosphorus 9.2 mg/dl, corrected calcium 9.9 mg/dl, albumin 2.7 g/dl. The patient's admission creatinine was 4.7 mg/dl, compared to the basal creatinine value of 0.88 mg/dl. Spot urine protein level: 694 mg/dl, spot urinary creatinine level: 142 mg/dl. The serum lambda light chain level was found to be 1720 mg/l, and the kappa light chain level was 32 mg/l. The ratio was 0.0189 (Kappa/lambda ratio: 0.26-1.65) and was evaluated for clonality impairment. Echocardiography reveiled left ventricular EF 45%, left ventricular global mild hypokinetic, hypertrophic cardiomyopathy. Left atrium dilatation, severe tricuspid insufficiency, pulmonary hypertension were reported as increased left ventricular myocardial brightness. Further investigation and examination were recommended due to findings suggestive of amyloidosis. In the bone marrow aspiration sampling, 15-20% of typical plasma cells and sporadic mott cells were seen.

Conclusion. Amyloidosis should be considered in the differential diagnosis, especially in individuals with nephrotic syndrome over the age of 40 with systemic disease findings.

PP-34 Should we prescribe individualisation dialysate sodium or not?

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Introduction. Pre-hemodialysis serum sodium levels can vary among patients, therefore, a single dialysate sodium prescription may not be appropriate for all patients. The aim of the study was to investigate whether dialysis patients will have some beneficial effects of prescription of different models of dialysate sodium.

Methods. 77 nondiabetic subjects performed 12 months hemodialysis (HD) sessions with dialysate sodium concentration set up at 138 mmol/L, followed by additional 3 models of dialysate sodium (each one 2 months sessions) wherein dialysate sodium was set up: model

1: according to pre-hemodialysis serum sodium concentration, model 2: sodium concentration in UF fluid, model 3: sodium profiling (144-136 mmol/L). Blood pressure (BP), interdialytic weight gain (IDWG), thirst score, sodium gradient were analysed. After the standard dialysate sodium hemodialyses, the subjects were divided into normotensive, hypertensive and hypotensive based on the average pre-hemodialysis systolic BP during the standard dialysate sodium hemodialyses.

Results. Model 1: resulted in significantly lower BP (153.60±14.26 versus 133.61±11.88 mmHg; p=0.000) and IDWG (2.21±0.93 versus 1.87±0.92 kg; p=0.018) in hypertensive patients, whereas normotensive patients showed only significant decrease in IDWG (p=0,004). Hypertensive patients had significant highest sodium gradient compared to other patients ($p<0.05$), followed by significant increase of 0.6% IDWG confirmed with univariate regression analysis. Thirst score was significantly lower in all patients with individualized-sodium HD. Model 2: resulted in significantly lower BP in normotensive and hypertensive patients, with no influence on IDWG and thirst score compared to standard dialysate sodium. Model 3: significantly higher BP and IDWG in all 3 groups and significantly higher thirst score in normo and hipotensive patients, with no influence in hypertensive patients.

Conclusion. Model 1 resulted in better clinical outcome in hypertensive and normotensive patients compared to standard dialysate sodium, whereas other 2 models didn't show any clinical benefits.

PP-35 Mortality and related risk factors of COVID-19 infection in hemodialysis patients-single center study

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Introduction. Dialysis patients appear to be at increased risk for viral infection next to an enhanced risk for mortality, even in the face of an often apparently mild clinical presentation. Immune systems may be responsible for a reduced antiviral response, whereas chronic activation of innate immune system and endothelial dysfunction provide background for a more severe course. The aim of this study was to provide evidence on Covid-19 incidence, mortality and determinant risk factors for the mortality of 54 infected patients of Hygeia Hemodialysis center based on clinical, laboratory, and radiologic findings.

Methods. This is a single-center, retrospective, observational study during the period July 2020-October 2021. This study included 53 dialysis patients confirmed to be infected by coronavirus, with positive in RT-PCR/ rapid test nasopharyngeal swab. Data are collected by files and included clinical, laboratories and radiological information.

Results. The incidence of Covid-19 infection in the center (160 patients) was very high 0.37 compared to the incidence in the general population. Of 54 patients, 10 patient died (18%), 16 (23%) patients were admitted at the hospital, 10 of them needed mechanical ventilation. Patients who died were older (mean age was 60+), had more comorbidities as diabetes (50%), COPD, CV disease (30%). Most of patients (78%) had radiological manifestation compatible with Covid pulmonary involvement, and 39% had severe radiological manifestation CO-RADS 5.

Conclusion. Hemodialysis patients are older and have more underlying diseases, they likely are more susceptible to severe acute respiratory syndrome Covid-19 pneumonia than general population, and have a high mortality rate. The presence of clinical severity of clinical presentation, high levels of ferritinemia in admission, decrease in platelet count in hospitalization may be used to predict the mortality risk of these patients.

PP-36 COVID 19 in primary care

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Introduction. Most people with coronavirus disease 2019 (COVID-19) develop mild or uncomplicated illness. Primary care has played an important role in the diagnosing and managing of COVID-19 reducing the demand for hospital services. The aim of this study was to evaluate the incidence and outcome of COVID-19 patients followed in the primary care setting.

Methods. This was an observational study during July-September 2021, in a primary health care center in Tirana Albania. Included were patients aged >18 years who tested positive for COVID-19 by polymerase chain reaction (PCR) or rapid test.

Results. During three month period 66 patients who asked the general practitioner consultation tested positive for the PCR or rapid test. Mean age was 42±10.5 years and 36% were male. 12% had comorbidities as diabetes mellitus 8%, Arterial Hypertension 62%, other 30%. The spectrum of symptoms was: fever 90%, cough 60%, tiredness 93%, loss of taste or smell 6%, muscle pains 89%, diarrhea 15%, red or irritated eyes 1.5%, difficulty breathing 3%. The situation aggravated in 2 cases and they needed hospitalization.

Conclusions. All over the world primary care physicians have been on the front line of the pandemic response. Primary care can provide important data to public health. The sustainable primary care with adequate resourcing can strengthen the capacity for essential services.

PP-37 Repeated syncopal event in a young female diagnosed with bilateral pulmonary tromboembolia: case report

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Introduction. Pulmonary embolism is a blockage of an artery in the lungs by thrombus. Virchow's triade of local trauma to the vessel wall, hypercoagulability and stasis of blood leads to thrombus formation in the leg veins. The most common sources of pulmonary emboli are the pelvic veins or deep veins of the thigh. The risk of blood clots is increased by cancer, prolonged bed rest, smoking, stroke, certain genetic conditions, estrogen-based medication, pregnancy, obesity, and after some types of surgery. Pulmonary emboli affect about 430,000 people each year in Europe. Rates are similar in males and females. Symptoms of a PE may include shortness of breath, chest pain particularly upon breathing in, and coughing up blood. On the other hand, syncope as a sign of pulmonary tromboembolia is an unusual clinical sign. In emergency department syncope accounts for 1% off all visits, and is a clinical sign of many diseases.
Case report. 19 years old female presented in emergency with a history of two episode of syncope, without a dyspnea and later diagnosed and treated as a case of pulmonary thromboembolism. At first, the diagnosis was suspected from the Cardiac ECHO (delated pulmonary artery 35mm, and PSAP 60mmHg), then confirmed with pulmonary angio-CT. Anamnesis vitae: the patient had been treated 4 years ago for a thrombophlebitis.
Conclusion. When a patient suffered a syncopal episode, pulmonary embolism must be considerd as a possible diagnosis.

PP-38 Acute kidney injury in leptospirosis. Be alert of this condition

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Introduction. Leptospirosisis is a zoonotic infection, spread all over the world caused by leptospira, a spirochete that mostly affects liver and kidney. A common complication that needs to be alert is Acute Kidney Injury (AKI), a life-threatening condition. It is characterized by tubular interstitial nephritis and tubular dysfunction. The most frequent form of leptospire nephropathy is hypokalemic and no oliguric form. We have studied the incidence of AKI in Albania along with the renal injury in two leptospiral phases.
Methods. 50 patients, diagnosed with Leptospirosis complicated with AKI were admitted at "Infection Diseases Department And Nephrology Department Of Mother Teresa Hospital" In Tirana between 2017-2020. All patients data were evaluated by their charts. Statistical analysis was performed using SPSS 20, Linear Regression. Elisa test was used for confirmation of leptospirosis infection and KDIGO classification for AKI diagnosis.
Results. Incidence Of AKI in Leptospirosis was 40%. 86% of patient were male. The most frequent age was 51-56 (51.4±12.69). Leptospirosis AKI was mostly hypokalemic and no oliguric. Mortality was 12% and only 16% of all patient needed hemodialysis treatment. Serum BUN, creatinine, bilirubin, potassium and thrombocytopenia levels were higher in acute phase than in immune phase. In the acute and immune phase WBC and PLT were independed risk factor of AKI $p>0.005$. Mean value of WBC in acute phase was 10416/mm3 and in immune phase 9056/mm3 ($p<0.003$). Mean value of PLT was 82000/mm^3 in acute phase and 190000/mm3 in immune phase ($p<0.0002$). In acute phase was a positive relation of bilirubinemia and azotemia $r=0.369$ and with creatinemia $r=0.339$ In immune phases there was a positive relation of bilirubin with azotemia ($r=0.882$) and creatinemia ($r=0.540$).
Conclusion. We concluded that AKI in leptospirosis is an actual problem for nephrologists in Albania and it is really important early and adequate treatment to have a good prognosis.

PP-39 Acute kidney injury induced by rhabdomyolysis caused by carnitine palmitoyltransferase ii deficiency - first reported case in two albanian brothers

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Introduction. Carnitine palmitoyltransferase II deficiency is an autosomal recessively inherited genetic metabolic disorder. It is characterized by an enzymatic defect that prevents long-chain fatty acid from being transported into the mitochondria for utilization as an energy source.
Case report. A 33 years old male patient was admitted to our hospital with muscle weakness, nausea and anuria. The patient mentioned he had performed excessive physical activity 3 days prior to hospitalization and feeling low back pain and muscle pain as well as lightly brown-colored urine. He then experienced anuria for about two days before arriving at the emergency unit. Six years ago, his older brother went through the same medical condition after a strenuous exercise. Physical examination and laboratory testing were performed at the admission. Blood screening revealed high serum levels of CK 64 180 U/L, CK-MB 1057 U/L, LDH 2890 U/L, AST 4017 U/L, ALT 1000 U/L, creatinine 6.6 mg/dl, urea 169 mg/dl. Kidney ultrasound showed normal kidneys in terms of size and structure. Other lab tests were within the normal range. The persistence of anuria and progressive declining of renal function were strong indicators to initiate dialysis treatment. The patient underwent eight hemodialysis sessions until the renal function was recovered. Genetic testing (molecular analyses) for our patient and his brother confirmed Carnitine palmitoyltransferase II deficiency. The patient was discharged from the hospital in good condition, with pro-

per recommendations regarding his lifestyle to prevent similar episodes in the future.
Conclusion. Patients showing myalgia, dark urine (brown/ redish/tea-coloured), high level of CK and development of AKI that require hemodialysis should be examined for inherited rhabdomyolysis induced by CPT II deficiency. Recognition of this condition can prevent further episodes of acute kidney injury.

PP-40 Metastatic renal cell carcinoma to the thyroid gland

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Introduction. The thyroid nodules are frequent in general population. The nodules are more prevalent in women and older age groups and detection are increased in people who underwent thyroid ultrasound. Metastasis to thyroid are rarely observed in the clinical practice.
Case report. A woman 42 years old present to the consultation for a solitary nodule to the right lobe of thyroid gland with dimensions 2.5 x 3 cm. The FNA-Biopsy of the nodule: Bethesda IV.
She referred than 8 years before left nephrectomy was done due to renal cell carcinoma. After the result of FNA- Biopsy confirmed the diagonosis total thyroidectomy was performed.The pathology findings was consistent with a solitary metastasis most compatible with a clear cell carcinoma from her previous renal carcinoma and the chronic lymphocytic thyroiditis. The immunohistochemistry findings ruled out primary thyroid cancer: CD-10 positive, EMA positive, Thyroglobulin negative, HBME-1 negative. The patient after surgery was treated with levothyroxine. One and a half months after thyroid surgery the PET-Scan was performed where focal 18-FDG uptake was seen in the thyroid bed, but did not find other metastasis. The ultrasound of the neck, did not detected thyroid tissues and without pathological lymph node. The lab results: TSH=5.9 mUI/ml; Ac TPO antibodies=90 UI/ml (normal range <70), Thyroglobulin <0.2 ng/ml (normal range 0-5); Thyroglobulin antibodies =32. UI/ml (normal range <70).
Conclusion. Solitary metastasis in the thyroid gland are rare, but they should be considered in a patient who have a history of renal carcinoma. Metastases in the thyroid gland can occur many years after removal of renal carcinoma.

PP-41 Anuria due to nephrolithiasis in autosomal dominant polycystic kidney disease (ADPKD) patient. A case report

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Introduction. Nephrolithiasis is frequent among ADPKD patients. Prevalence ranges between 13.3% to 58% in patients with ADPKD but its diagnosis can be challenging.
Case report. A 58 year old female, CDK stage III-A secondary to ADPKD present in emergency unit with: back lower pain, fever, severe dyspnea, strong chest pain, anuria. Results of examinations: RBC: 4.570.00 mm3, HGB: 11.7g/dl, HCT: 35.7%**,** WBC: 21.500 mm3, PLT: 44.000 mm3, urea: 136 mg/dl, creatinine: 5.21 mg/dl, D-Dimer: 12.8 mg/dl (0.2-0.5), total protein: 5.3 g/dl, albumine: 2,9 mg/dl, uric acid: 10 mg/dl, calcium: 8,7 mg/dl, potassium: 3.9 mg/dl, procalcitonine: 0.41 ng/ml, ferritine: 302 ng/ml, CRP: 16,08 mg/dl, LDH: 377U/L, fibrinogen: 600 mg/dl, PT: 110, INR: 0.94, Urine: pH 6.0, protein: 25 mg/dl, erythrocyte: 99, leukocyte: 85, bacteria 30. Abdominal ultrasound showed large volume of the kidneys with multiple cysts and hepatic cysts but missed kidney stones. Due to clinical signs and high D-Dimer levels she underwent Pulmonary Angio CT Scan which excluded Pulmonary Thromboembolism. Computerized tomography (CT) without contrast showed a 6mm stone in kidney pelvis complicated with hydronephrosis. After performing a hemodialysis session the patient had diuresis and the polyuria phase lasted 10 days. She was discharged after 4 weeks of hospitalization in very good health and optimal renal function: urea 51.7 mg/dl and creatinine 1.54 mg/dl. She had normal renal function urea 40mg/dl and creatinine 1.2mg/dl at her last updated follow up 3 months after discharged.
Conclusion. Nephrolithiasis should be kept in mind in ADPKD patients with liver cysts, upper urinary tract obstruction and hematuria. Early diagnosis and accurate management of the renal stones in ADPKD are important to prevent progression to ESRD and acute decline in renal function.

PP-42 Acute kidney injury from COVID-19 in a patient with chronic kidney disease stage III-A, who underwent a successful kidney transplant. A case report

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Introduciton. Acute kidney injury (AKI) is routinely diagnosed in hospitalized patients due to COVID-19 but in Chronic Kidney Disease (CKD), such a high risk population, complication with AKI is a strong predictor of end stage renal disease (ESRD) who needs renal replacement therapy to be resolved.
Case report. A 46 year old male had CKD stage III-A secondary to hypertension by 7 years. On July 2020 he tested positive to COVID-19 and was treated successfully at home. Three months later he presented with hematuria, fatigue and myalgia. Results of examinations: RBC: 3.040.000 mm3, HGB: 9.1g/dl, HCT: 24.8%, PLT: 330.000 mm3, WBC: 9300 mm3, PCR: 55.5 (1-8), fibrinogen: 611mg/dl (169-515), PT: 61.9% (70-120), INR: 1.36 (0.7-1.2), urea: 225mg/dl (10-43), creatinine:

8.5 mg/dl (0.5-1.2), uric acid: 8.6 mg/dl (2.6-7.2), phosphorus: 6.8mg/dl (2.5-4.5), cholesterol: 116mg/dl (140-220), TG: 31 mg/dl (50-150), Alb: 3.1 g/dl (3.5-5.2), eGFR 9 ml/min/1.73 m^2. Albuminuria/24h: 2.48g% CT lungs-abdomen: 3-4 focal density in both lungs due to COVID-19 and chronic damage in both kidneys. We confermed ESRD and dialysis was recommended. The patient refused it so we worked up for live related kidney transplant. He underwent a successfully kidney transplant after three months of initial diagnosis of COVID-19. Basiliximab induction with triple drug imunossupression consisting of prednisone, tacrolimus and mycofenolate mofetil was used. He was discharged with a normal graft function. He remains so at last updated follow up 11 months post transplant with an eGFR of 93 ml/min/1.73 m^2.

Conclusion. We report this case for guiding clinical nephrologists to several concrete steps to prepare for our collective new normal in coming, for our high risk patients in the setting of a global pandemic.

PP-43 Comorbid factors for early mortality in myeloma-related kidney disease. Case series study

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Introduction. Renal impairment (RI) is an independent predictor of poor survival outcomes in multiple myeloma (MM). In the first year, significant early mortality (EM) was determined in patients with MM who underwent Hemodialysis treatment. The aim of the study was to evaluate the EM rate and investigate the risk factors associated with EM in MM patients.

Methods. The study was held in the hematology unit of UHC "Mother Teresa" during January 2020-March 2021. Out of 183 patients, 33.3% have in presentation Myeloma-Related Kidney Disease (MRKD).

Results. We evaluated 61patients with MRKD, 67.2% men, the mean age 66.2±8.7 years old, and 19.7% of patients needed hemodialysis support. The one-year mortality rate in MRKD was found 29.5% ($p<0.01$), and the EM rate (the first 100 days of diagnosis) 13.1% while 62.5% of them underwent hemodialysis treatment. During follow-up, 10% of patients with MRKD had confirmed positive SARS-CoV2 tests, associated with a high mortality rate of around 67%. Univariate logistic regression identified GFR<30ml/min ($p<0.01$), hemodialysis treatment ($p<0.01$) and creatinine >2 mg/dl ($p=0.01$) as risk factors for mortality. Multivariate logistic regression found creatinine >2 mg/dl, GFR <30 ml/min, hemodialysis, Covid-19 infection and hypoalbuminemia remained independent predictors of high mortality in MRKD patients after adjusted for cofounders.

Conclusion. A high mortality rate resulted in MRKD infected with Covid-19. RI is the second most common cause, after infection, of EM in MM patients. It is potentially reversible, so it is of high interest early diagnosis and management of MRKD for more prolonged survival. Prophylactic measures in patients with preexisting kidney failure may further reduce this risk.

PP-44 A rare atypical hus following biontech vaccination for COVID

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Introduction. Atypical hemolytic-uremic syndrome (aHUS) is a disease that primarily affects kidney function. It is characterized by the triad of thrombocytopenia, microangiopathic hemolytic anemia, and acute renal failure. A variety of precipitating events have been associated with aHUS including infections, drugs, autoimmune conditions, transplants, pregnancy, and metabolic conditions.

Case report. A previously healthy 19 year old woman admitted to the hospital with sudden onset of bloody diarrhea 2 days after Biontech vaccination, physical examination was revealed no any pathological sign except bloody diarrhea. Colonoscopy was performed promptly and it was resulted with severe colitis. In the arterial and venous phase of CT image hypodense micro-thrombus was observed and transverse colon biopsy was characterized with ischemic colitis. There was no parasite/Adenovirus/Rotavirus/Shiga toxin in the stool tests. Hemoglobin and platelets dropped from 13.2 to 5.3/186000 to 22000. Haptoglobin level was 0.08; the lactic acid dehydrogenase was elevated at 1119. Peripheral smear showed 2% schistocytes. ADAMTS 13 was positive at 88%, fibrinogen level was normal and Coombs was negative so TTP and DIC were excluded. 1 mg/kg/day steroid and IVIG therapy was started but the patient had not improved with this therapy and 2 times plasmapheresis were administerd. Then, the patient showed evidence of hematological and renal remission, with improvement in platelet 260000, creatinine level 1.9 mg/dl and LDH level trending down to 614U/L after plasmapheresis. While still awaiting the genetic study results, we started the patient on eculizumab treatment because of the suspected aHUS. The patient was also administered the meningitis vaccine for meningitis prevention and was started on penicillin prophylaxis before initiation of the eculizumab therapy. After 28 days of eculizumab therapy, the serum creatinine reached to baseline level 0.9 mg/dL.

Conclusion. Atypical HUS has a poor prognosis eventually leading many patients to require dialysis and there are many etiological factors for this disease. While the coronavirüs infections and vaccinations with Biontech

are so common, we want to call attention to the Biontech vaccination may be a precipitating factor for aHUS.

PP-45 Evaluating urinary albumin excretion after kidney donation

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Intorduction. Living donor kidney transplantation has become an important treatment option for ESRD patients. In our country, for more than two decades now, we have a growing number of individuals donating kidney to relatives. The aim of this study was to assess the role of nephrectomy as an independent risk factor for the development of microalbuminuria after donating a kidney for transplant.

Methods. Between 1993 to 2017, 269 patients with ESRD have received a kidney transplant from a living donor in Albania. Among them, 70 donors accepted to participate in the study. Urine and blood samples were collected for further examination. Urinary albumin excretion rate was calculated according to the albumin to creatinine ratio in an early-morning urine sample. The CKD-EPI formula was used to calculate GFR.

Results. There were a total of 70 kidney donors participating in the study, 73% female and 27% male. The average time after donation was 10±5.6 years ranging from 4 to 28 years. The mean age at the time of nephrectomy was 49.3±10.2 years. The prevalence of microalbuminuria was 24.3%, female had a higher risk (ratio F:M, 2.7:1). There was a negative correlation between microalbuminuria and eGRF, r:-0.33($p<0.01$), higher level of microalbuminuria was associated with decrease of eGFR. There was no association with age, BMI and blood pressure. Microalbuminuria was present only in 21.1% of 19 obese donors and in 28.1% kidney donors with hypertension.

Conclusion. We found that kidney donation is associated with a modest increase in albuminuria parallel to a gradual and moderate decrease in eGFR. The risk after donating the kidney is minimal for the donor but the long-term follow-up is necessary for all living kidney donors in order to minimize harmful effect.

PP-46 Correlation of systolic left and right ventricle with pulmonary hypertension and their impact on survival in dialysis patients

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Introduction. Pulmonary hypertension (PH) is lately known as a complication of chronic kidney disease. The present study aimed to determine the impact of systolic left and right ventricle on PH and dialysis patients' survival.

Methods. We studied 125 stable hemodialysis and peritoneal patients (females 40%, mean age 52.42±11.88 years) on renal replacement therapy (RRT) for more than 3 months with a follow of 2 years. After conventional echocardiographic examination, a tissue Doppler echocardiographic (TDE) examination was performed to evaluate the global and regional myocardial systolic function and pulmonary hypertension. The peak systolic velocity at the lateral mitral annulus (MASa cm/s) and the peak systolic velocity at the lateral tricuspid annulus (TASa cm/s) were used as a marker of LV systolic function and RV systolic function, respectively. PH was defined as systolic pulmonary artery pressure (sPAP ≥35 mmHg). Logistic regression analysis was used to evaluate the risk factor for PH and its impact on survival.

Results. According to the echocardiographic findings, PH was found in 28% (35 patients) of all patients. Mean PH was 33.46±5.38 mmHg. The lower left ventricular ejection fraction (EF), peak systolic velocity at the lateral mitral annulus (MASa), and the peak systolic velocity at the lateral tricuspid annulus (TASa) were correlated and found predictors of PH. The cardiovascular mortality rate was 15.5%. In ROC analysis for CV mortality, the area under the curve (AUC) for PH was found 0.8; while the inverse relationship was found with MASa and TASa with AUC=0.66 and 0.95, respectively.

Conclusion. Our study shows that PH is frequent in dialysis patients. It is influenced by nontraditional risk factors in CKD associated with the diastolic and systolic left and right ventricle dysfunction. The evolution from an LV phenotype to an RV phenotype over time due to PH requires further investigation. Easy to implement, cardiac imaging at the bedside and in outpatient clinics offers a positive perspective in the early diagnosis of cardiac abnormalities and the nearest approach to this condition, so it is highly recommended in the dialysis population.

PP-47 Alkaline phosphatase a traditional marker of vaskular calcifications in patients with dialitic therapy

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Introduction. Alkaline phosphatase degrades pyrophosphate, which is a potent inhibitor of vascular calcification. The aim of this study was to evaluate the association of ALP with vascular calcifications in patients with hemodialysis and peritoneal dialysis.

Methods. The cross-sectional study was conducted. The study involved 45 patients in HD and 36 patients in PD. The collection of biochemical data and the identification of vascular calcifications through anterior-posterior radiographs of the abdomen and hands were performed. To evaluate vascular calcification Adragao score was used.

Results. Vascular calcification was present in 66.7% of the total population, 60% in patients on hemodialysis treatment and 75% in patients with peritoneal dialysis

treatment. The average calcification score according to Adragao was 2.86, 2.64 in HD patients and 3.14 in DP patients. The mean ALP level in patients with calcifications was higher 195.6 (±92.9) compared with patients without calcifications 107.9 (±85.6) with significant statistical difference between them, p=0.01. The categorical division of ALPs >120 UI/ml and ALPs ≤120 UI/ml saw a significant trend in increasing the percentage of calcifications. ALP>120 UI/ml was significant and independent factor for predicting vascular calcifications in univariate analysis with OR=6.14, 95% CI reliability interval, p<0.01 and in multivariate logistic regression analysis with OR=1.21, 95% CI reliability interval, p=0.02. The time on dialysis in patients with calcifications was longer compared to patients without calcifications.

Conclusions. Alkaline phosphatase is a predictor of vascular calcification in patients undergoing hemodialysis and peritoneal dialysis. ALP can be used in clinical practice as a common, traditional marker of clinical manifestations of vascular calcification

PP-48 Conservative management and outcome of multiple fractures in hemodialysis patients (case report)

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Introduction. Between major complications of renal failure, mineral and bone disorder (MBD) develops at early stage but symptoms manifest later starting with bone and joint pains and fractures. Bone fractures, at any skeletal site occur more frequently in haemodialysis (HD) patients than in the general population. Surgical treatment of femoral neck fractures is usually performed for a better and quick outcome.

Case report. The patient was a 42-year-old man, under chronic HD treatment for 7 years. The primary diagnosis was Alport syndrome. High serum PTH level persisted since the beginning of HD treatment, but the use of cinacalcet was not regular. An earlier fracture was corrected by hip arthroplasty dexter. The patient subsequently fell off and was unable to move. He was brought to the emergency department, and a total body computer tomography revealed: compressive fractures of thoracic vertebras T8, T9; proximal humeral fracture; left intertrochanteric hip fractures. Laboratory data showed a high levels of PTH (2200 pg/ml), serum calcium (9.4 mg/dL), hyperphosphatemia (7 mg/dL), and elevated alkaline phosphatase activity (273 U/dL).

Orthopaedic surgeons did not reach in a decision to proceed with surgery. Conservative treatment was accepted as an option and the patient was transferred to the nephrology department. During 4 months he remained hospitalized, being unable to move and stayed in bed. One month after discharge from hospital he could be sitted in a wheelchair. Pain diminished and radiograph showed bone union was obtained for the proximal humeral fracture and compressive fractures of thoracic vertebras, but not for the left femoral neck fracture. Environmental adjustment was required and a nursing-care service also.

Conclusion. Surgical treatment for a femoral neck fracture is generally indicated unless the patient has significant comorbidities that present an unacceptable risk. Conservative treatment may be acceptable, but requires a long period of bed rest and it negatively influences patients' activities of daily living (ADL) and quality of life (QOL).

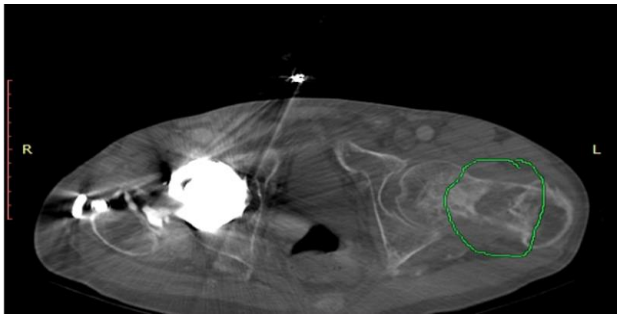

Fig. 1. Hip arthroplasty dexter and left intertrochanteric hip fractures

PP-49 Incidence and outcome of acute kidney injury in infectious disease

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Introduction. A rise in the incidence of acute kidney injury (AKI) has been reported in the last decades. The aim was to evaluate the incidence of AKI in infectious disease setting, factors associated with AKI, outcome and prognostic factors.

Methods. This is an observational study of 112 patients hospitalized in the infectious disease department, during a 6 months period (January-June 2019). AKI was defined according to KDIGO. Adult patients (age ≥18 years), who stayed longer than 48 hours in hospital were included. Transplanted and chronic dialysis patients before admission were excluded.

Results. During the study period 112 patients completed inclusion criteria. The mean age was 45.8±20.5 years and 64.3% were male patients. According to the KDIGO criteria 39.3% patients met criteria for AKI during the study period and were classified as non AKI 60.7%, stage I 22.3%, stage II 6.3%, and stage III 10.7%. In 75% cases AKI was present at admission. 43.7% of patients had comorbidities as. AKI patients were aged, 55±16 years vs. non AKI patients 39±19 years; p<0.001 and had more comorbidities: AKI 53% vs. non AKI 28%, p=0.008.Overall in-hospital mortality was 13.3%. AKI patients had significantly higher mortality rate (AKI 22.2% vs. non AKI 7.5% p=0.025) and longer hospital stay (AKI 8.3±5.5 vs. non AKI 5.5±3.8 p=0.002). Logistic Regression analysis showed as independent factor associated with AKI advanced age OR=1.04; CI 1.01-1.07; p=0.002. Cox Regression analy-

sis showed AKI was independent factor associated with mortality in ICU OR=1.7; CI 1.06-2.92; p=0.028.
Conclusions. High incidence of AKI was found between patients with infective disease. AKI patients were aged and had significantly more comorbidity. Advanced age was found independent factor associated with AKI. AKI was independent factor associated with mortality in ICU.

PP-50 The prevalence of cognitive impairment and related risk factors in CKD population

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Introduction. Cognitive impairment (CI) is an increasingly identified significant cause of chronic disability seen in patients with chronic kidney disease (CKD). Our study aimed to evaluate the prevalence of CI, in CKD stage 4-5 patients, Hemodialysis, Peritoneal dialysis, and Transplant patients and evaluating their underlying risk factors.
Methods. This is a cross-section study evaluating 167 patients who met the inclusion criteria in the study. Of these, 39% were on hemodialysis, 22% on peritoneal dialysis, 19% on transplant, and 20% with CKD stage IV-V. Cognitive impairment in the study population was assessed based on the MoCA test. Patients with a MoCA global score of 24/30 were considered cognitively impaired. The rating is classified: light, moderate, heavy, and very heavy.
Results. The frequency of CFK based on the test classification was 20% mild, 61% moderate, 15% severe, and 3% very severe. In the studied population, it was observed that there is a significant relationship between cognitive impairment and forms of renal replacement therapy ($p<0.001$) and the etiology of the underlying disease, p=0.0011). The multivariate linear regression test shows an independent relationship of CI with age, where each increase of 1 year in age leads to a decrease of 0.094 points of the MoCA test. Besides, it was observed that there is a significant negative correlation of CI with the degree of calcification in HD and DP, with the serial level of magnesium and ALP in the whole population, and a positive correlation with serum Ca and hemoglobin.
Conclusion. In this study, we saw the impact of CKD and RRT on the relatively high prevalence of CI. Our results showed that bone biomarkers, vascular calcification score, and age contribute and are independently associated with longitudinal changes in some domains of cognitive function in patients with CKD going in parallel with the pathogenesis of vascular and Alzheimer's dementia.

PP-51 The impact of bone biomarkers in cognitive impairment in hemodialysis and peritoneal dialysis patients

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Introduction. Patients undergoing dialysis have a higher risk of cognitive impairment (CI) than the general population. We evaluated the association of bone biomarkers on cognitive function in hemodialysis (HD) and peritoneal dialysis patients (PD).
Methods. A cross-section study evaluated 105 patients who met the inclusion criteria in the study. Of these, 65.7% were on hemodialysis, 43.7% were females, and the mean age was 53.6±11.3 years. Cognitive impairment in the study population was assessed based on the MoCA test. Patients with a MoCA global score of 24/30 were considered cognitively impaired. A simple vascular calcification score (SVCS by Adragao) based on plain radiographic films of the pelvis and hands was used to assess vascular calcification.
Results. There was no found difference in mean MoCa score between HD and PD group (the mean MoCA score for HD was 22.7±4.7and in PD group 20.23±5.8, p=0.06) where the mean VCS was found higher in PD group (2.43±2.67 and 3.2±4.3 respectively (p=0,024). The HD group showed a relationship between low MoCA score and high calcification score (p=0.032), low level of PTH (p=0.008), and low level of ALP (p=0.001), wherein PD group also stayed the relationship between low MoCA score and calcification score (p=0.04) but was found with high calcium level too (p=0.022). The multivariate linear regression test shows an independent relationship of CI degree of calcification in HD and DP (p=0.03).
Conclusion. In this study, we found a strong relationship between vascular calcification and low MoCA score, parallel with the pathogenesis of vascular and Alzheimer's dementia.

PP-52 IgA nephropathy and spinal epidural abscess after covid-19 infection: a case report

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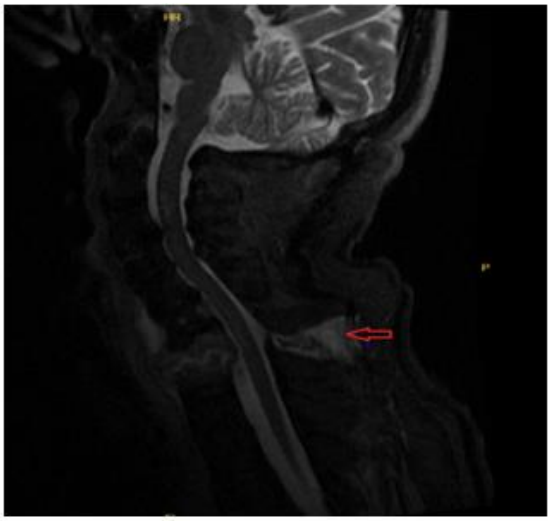
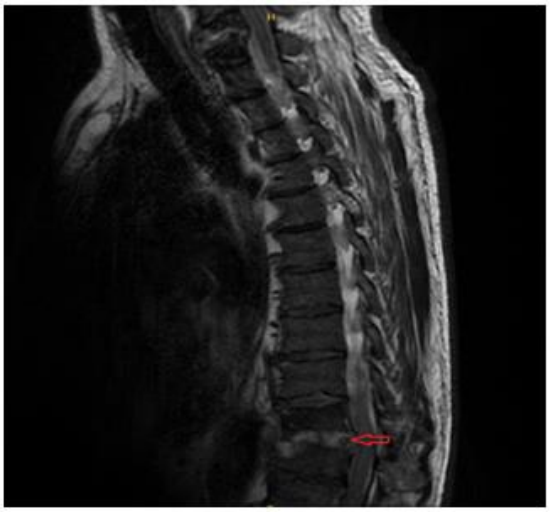
Introduction. Although COVID-19 preferably affects the respiratory systems, some patients present with neurological symptoms such as acute inflammation of the brain, spinal cord, and meninges. Based on recent studies acute kidney injury (AKI) is also a well-documented complication of COVID-19. In this paper we

report a case presented with epidural abscess and Ig A nephropathy with AKI. The aim of our report is to provide our experience with people who are experiencing multiple and serious complications after COVID-19.

Case report. A 56-year-old male admitted to the hospital for generalized weakness and fever. He was treated in hospital for ten days with COVID-19. He did not receive any immunosuppressive therapy during admission. One day after his discharge he experienced back pain and received analgesic therapy for ten days. One month later, he experienced severe back pain and gross hematuria. He was admitted to hospital. Laboratory findings revealed AKI with serum creatinine 4.83 mg/dL (reference: 0.7-1.3 mg/dL), anemia and lymphopenia. His renal biopsy revealed IgA nephropathy and thoracic Magnetic resonance imaging (MRI) of cervical-thoracic-lumbar spine with contrast showed circumferential enhancement around the C7-T1 and T10-T11 vertebral bodies, and moderate anterior-posterior epidural enhancement with cord-compression consistent with epidural abscess (Figure 1A and 1B).



1A. Lesions compatible with epidural abscess are observed in C7 - T1 bodies.(arrow)



1B. Lesions compatible with epidural abscess are observed in T10 - T11 bodies.(arrow)

Fig. 1. MRI thoracic and cervical spine with contrast
MRI, Magnetic resonance imaging; C, cervical spine; T, thoracic spine

Conclusion. We hope that this report helps healthcare professionals to be aware of the heterogenous neurological and renal complications of COVID-19. Clinicians must be alert to potential complications during or after the diagnosis and treatment of patients with COVID-19.

PP-53 Nutcracer syndrome - case report

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Introduction. Nutcracker syndrome (NCS) is a vascular compression disorder of the left renal vein between the superior mesenteric artery (SMA) and aorta. The most common clinical features are intermittent hematuria, proteinuria, left flank pain and gonadal varices, alongside with the diagnostic imaging features of the anatomy associated with the syndrome.

Case report. We report the case of a 46 y/o woman who was admitted at hospital for a two years history of abdominal pain and intermittent hematuria. Physical examination revealed left flank tenderness, BP of 110/70 mmHg and HR of 85 bpm with regular sinus rhythm. Laboratory results on admission showed: WBC: 7.07x 10^3 mm^3, RBC: 3.92x10^6 mm^3, HGB: 10.1 gr/dl, PLT: 267x10^3 mm^3, ESR: 27mm/h, Creatinine: 0.9mg/dl, Urea: 30mg/dl. Urinalysis revealed: 20-30 RBC per high power field and protein 25mg/dl. Abdominal US revealed a distended left renal vein. Cystoscopy resulted normal. Abdominal CECT confirmed the left renal vein distention up to 9 mm in caliper with an abrupt diameter reduction of 2.3 mm at the AOM angle. High compression ratio (3.9) with narrowing of the AOM angle (18º) and shortening of the AOM distance (6 mm), were consistent with anterior NCS.

Conclusion. NCS refers to the compression of the left renal vein between the SMA and aorta. Dilatation of the proximal portion of the vessel due to increased pressure gradient with resultant venous hypertension and rupture of the thin-walled veins into the collective system is the mainstay of hematuria (from the left ureteral orifice only). Other clinical features of NCS are left flank pain, pelvic pain and gonadal varices. Orthostatic proteinuria has also been reported. This is a rare syndrome but to be considered in case of hematuria of unknown origin.

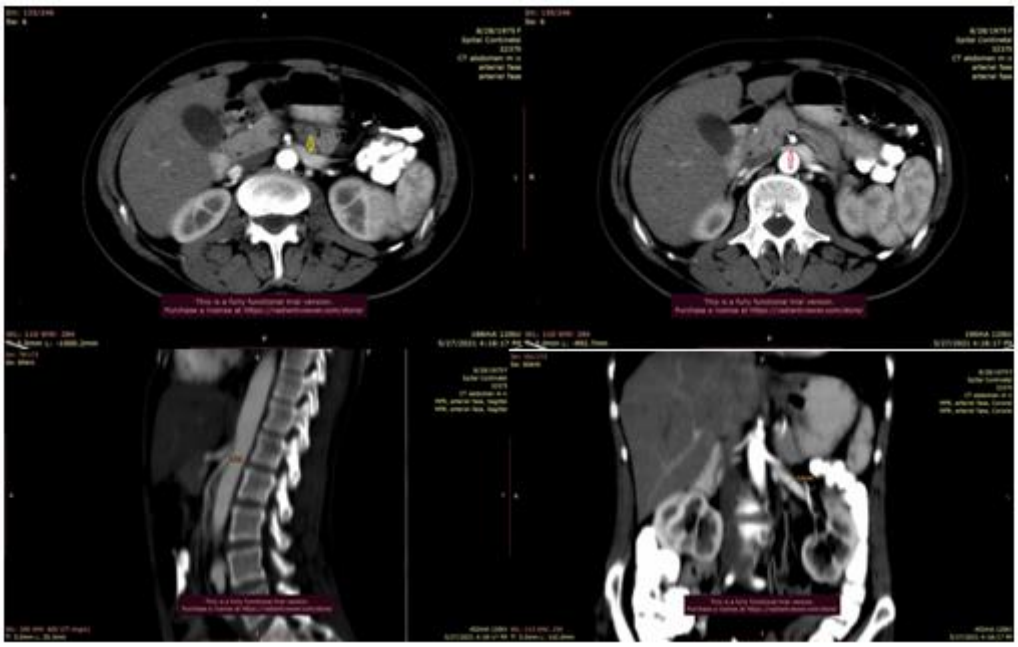

Fig. 1. Diagnostic imaging features of the anatomy associated with the NCS.

PP-54 Performance of renal function in patients treated with Sacubitril/Valsartan

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Introduction. Chronic kidney disease (CKD) is highly prevalent in patients with chronic heart failure (CHF) and increase the risk of cardiovascular mortality. They both are part of Cardiorenal Syndrome. Sacubitril/ Valsartan is the first in class angiotensin receptor-neprilysin inhibitors which reduce the risk of cardiovascular mortality compared with ACE-I in patients with heart failure with reduced ejection fraction. The purpose of this study is to describe and evaluate the performance, changes and tolerance in renal function in patients treated with Sacubitril/Valsartan and to evaluate the tolerance assessment by patients with renal replacement therapy.

Methods. This study is a retrospective observation and involved 53 patients with CHF with reduced ejection fraction and CKD, 9 of them were undergoing treatment with renal replacement therapy (hemodialysis). All patients were treated with Sacubitril/Valsartan, for a minimum of 3 months. The mean and standard deviation for the continuous variables were calculated and the statistical progressing was performed through, ANOVA test, non-parametric Friedman test, Hi-square statistical test (X^2).

Results. Fifty three patients were involved in the study. The mean age of the patients included in the study was 64.94±14.05 years and the highest percentage were men (81.1%). Patients were treated with different doses of Sacubitril/Valsartan, and the most frequent dose was 100 mg daily which was well tolerated by patients in the age group of 55-64 years. Sacubitril/Valsartan was well tolerated by patients of hemodialysis without showing hypotension.

Conclusion. Sacubitril/Valsartan is well tolerated by patients with Cardiorenal Syndrome. It improves their symptoms, improves the renal function and values of nitrogen, creatinine, GFR will be related statistically with the dose of use.

PP-55 What strategy should we take to prevent the CKD and its complications based on the 2 year experience in management of a hemodialysis center?

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Introduction. Chronic kidney disease (CKD) is a progressive pathology which affects 5-15% of the population worldwide. Its trend is seen to be increasing in the last 10 years, a trend which has been also observed in the Albanian population.

Methods. This is a retrospective study, with descriptive and analytical character. The data came from medical records of patients who have received chronic health care at the hemodialysis service during 2019 in the regional hospital of Gjirokastra. These data have been re-evaluated. Patients are followed periodically every month with examinations according to the protocol approved by the Ministry of Health and Social Protection of Albanian Republic.

Results. The study population consisted of 46 patients who received chronic hemodialysis service at our hemodialysis center during 2019. The average age of chronic patients was 60.9 years with a predominance of the

age group 61-80 years respectively 48%. Mostly they were men (63%) while women were only 37% of the total number of chronic patients. Patient's survival more than 14 years was only 7%. Hypertension was observed in 65% of patients of which 94% were male while 9% suffered from diabetes mellitus of which 75% were male. The most commonly used vascular access was native arteriovenous fistula in 87% of patients while 6 patients received this service through central venous catheters (4 patients with permanent catheter and 2 patients with temporary catheter). But their first vasal access at the start of hemodialysis (HD) had been a temporary central venous catheter in 80% of the patients.
Conclusion. Prevention of kidney disease should have as a priority the information of population around these pathologies. It is necessary to create an information strategy of the population using mini-discussion sessions at the workplaces and schools, distributing information brochures or using the media or social applications to promote an active healthy lifestyle, a healthy diet and the importance of check-up.

PP-56 The impact of COVID-19 on dialysis dependant patients: a single centre experience
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Introduction. As of March 2021, coronavirus disease 19 (COVID-19) outbreak has been reported in Serbia. Due to high numbers of infected overall population and increased risk of transmission within dialysis population, COVID-19 greatly affected management of dialysis centres and urged quick reorganization.
Methods. Given above, during the first 12 months of the pandemic in Serbia, Clinical Hospital Centre (CHC) Zemun in Belgrade, worked solely with COVID-19 patients. 106 of haemodialysis (HD) and 34 peritoneal dialysis (PD) patients were referred to other dialysis centres. At the same time, 192 dialysis dependant patients (121 men, 67±13 years old) were treated in CHC Zemun due to COVID-19. Out of these 192 patients, 141 (73.4 %) were chronic HD patients from different dialysis centres, 4(2.1 %) were PD patients, 28(14.6 %) received haemodialysis due to acute kidney injury (AKI) and 19 (9.9%) due to worsening chronic kidney disease (CKD).
Results. Mean hospitalisation duration was 13±8 days. Radiography verified bilateral pneumonia in 148 patients, unilateral pneumonia in 18 and 26 patients had no signs of pneumonia. One third of the dialysis dependant patients did not require oxygen support throughout hospitalisation, while others received either high-flow oxygen via nasal mask, non-invasive or invasive mechanical ventilation. Mortality rate among followed patients was high, precisely occurred in 64 (33%) of overall patients, including mortality of AKI dialysis dependent patients 34 (17.7%). Among other complications, fistula thrombosis occurred in 14(7.3 %) patients during hospitalisation and sepsis in 17(8.8 %).
Conclusion. COVID-19 in dialysis dependant patients increases risk of severe complications, including high mortality rate.

PP-57 The prevalence of kidney injury and related risk factors in multiple myeloma patients
Saraci A, Cadri V, Pasko N, Imeraj M, Toska L, Strakosha A, Rista E, Collaku K, Cili A, Ivanaj A and Barbullushi M
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Introduction. Kidney injury (KI) affects up to 50% of patients with multiple myeloma (MM) and is considered a very common and severe complication of MM. The aim of the study was to estimate incidence and prevalence of KI in MM, evidence of the type and time of onset of KI.
Methods. A retrospective study of 183 MM patients under specific treatment at Hematology Unit of UHC "Mother Teresa" from January 2020-March 2021.
Results. Prevalence of KI in MM was33.3%, 67.2% men, and the mean age 63.7 (9.3) years. During a median follow up of 15 months 22.9% experienced acute kidney injury (AKI) and 10.3% of MM patients experienced chronic kidney disease (CKD) ($p<0.01$). 41% of new MM have creatinine level >2 mg/dl at presentation while 7.1% manifest KI during the course of the disease. Significant precipitating factors resulted: hypercalcemia (31.1%), nephrotoxic drugs NSAIDs (16.4%), ACE/ARB (11.5%), dehydration (11.5%) and Covid-19 (9.8%). 31.1% of them have more than one precipitating factor. During the first month of specific treatment to the underlying disease, improvement in renal function was observed in 36.1% of patients ($p=0.02$). The multivariate linear regression test shows an independent risk factor of severe outcome of creatinine level >2 mg/dl and severe inflammation while treatment of MM with VED is an independent protective factor.
Conclusions. We found high incidence and prevalence of KI in MM and AKI is the main form of clinical manifestation. Improvement of renal function in the first month of treatment is seen by avoiding precipitating factors. Early identification of KI in MMis associated with a better prognosis of the underlying disease.

PP-58 Echocardiographic changes in asymptomatic prevalent hemodialysis population
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Introduction. Despite the high incidence of cardiovascular diseases in the dialysis population, screening in asymptomatic patients is not routinely used in clinical practice, except in those examined for kidney transplantation. Looking for signs of heart failure (HF), we

conducted a study to examine echocardiographic changes in prevalent hemodialysis (HD) patients regardless of symptoms.

Methods. Study involved 96 HD patients. Their data were collected from the medical records. To classify the severity of HF New York Heart Association (NYHA) functional classification was used. Echocardiographic examination was performed before HD.

Results. HF was found in 63(65.6%) patients: in 21 patients with reduced EF <50 % (HFrEF) and 42 patients with preserved EF ≥50% (HFpEF), plus remaining 33 patients with no HF (control group). More than 80% of patients from HFpEF and control group and 60% of patients with HFrEF had no or mild HF symptoms (NYHA classes 1 and 2). NYHA class 3 was found in 29% of patients with HFrEF, 19% in group 2 with HFpEF and 12% in group 3 without HF (NS). Further, NYHA was not selected as HF predictor. In addition to the echocardiographic HF findings, all patients with HF had the most pronounced left ventricular (LV) and atrial (LA) hypertrophy and diameter compared to patients without HF. Nevertheless, almost half of patients without HF had LV hypertrophy, increased diameter and volume overload of LA.

Conclusion. Although 65.6% of patients fulfilled criteria, most of them were asymptomatic for HF. Therefore, it is advisable to perform regular echocardiographic and cardiac examinations in all patients from the beginning of HD treatment regardless of their symptoms.

PP-59 Renal pathology in the region of municipality of Gostivar/1997-2021

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Introduction. Kidney diseases take significant place among the chronic non-transmissible diseases. Terminal damage of the kidneys in most of the cases begins slowly and insidious. The chronic kidney's insufficiency is a lifelong painful condition related with frequent controls, regular dialysis or transplantation.

The correct incidence and prevalence of the kidney diseases and kidney insufficiency is well known. From 1997 till 2021, the number of hospitalized patients has been growing. The number of patients going on dialysis have increased almost double. Looking at 1997, the number of patients being treated was 47, and in 2021, the number is 155, not including the patients, which on average of 7 to 10 have passed away on yearly basis. The rate of hospitalized patients registered with sickness morbidity is on average of 3.05 in the analyzed period. According to the gender statistics, most frequent patients are males, while according to the age, from 25 to 65 years. Most common diseases: nephrolithiasis N20/N23/46.6%, hypertension I 10/ 11.5%, Diabetes mellitus E11/ 19.8%.

Main emphasis at the kidney diseases should be put on prevention, while on second place, primary and secondary protection.

Index of authors

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EXAMPLES

1. Madaio MP. Renal biopsy. *Kidney Int* 1990; 38: 529-543

Books:

2. Roberts NK. *The cardiac conducting system and the His bundle electrogram.* Appleton-Century-Crofts, New York, NY: 1981; 49-56

Chapters:

3. Rycroft RJG, Calnan CD. Facial rashes among visual display unit (VDU) operators. In: Pearce BG, ed. *Health hazards of VDUs.* Wiley, London, UK: 1984; 13-15

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