ACU Sağlık Bil Derg 2019; 10(2):135-141
https://doi.org/10.31067/0.2019.135

Upper Gastrointestinal Disorders Among Dialysis Patients

Şafak Kızıltaş[1], **Sevgi Şahin**[2]

[1]Acıbadem University, Gastroenterology, Istanbul, Turkey
[2]Acıbadem University, Nephrology, Istanbul, Turkey

Şafak Kızıltaş, Prof. Dr.
Sevgi Şahin, Prof. Dr.

Correspondence:
Prof. Dr. Şafak Kızıltaş
Acıbadem University, Gastroenterology, Istanbul, Turkey
Phone: +90 532 573 13 18
E-mail: safakkiziltas@hotmail.com

Received : September 03, 2017
Revised : September 03, 2017
Accepted : December 17, 2017

ABSTRACT

The prevalence of co-morbid gastrointestinal symptoms is high in dialysis patients, and dyspeptic symptoms, such as nausea, vomiting, and epigastric burning are the most common symptoms. Upper gastrointestinal disorders (e.g., peptic ulcer disease and gastroparesis) underlie most of these symptoms, while less common but severe complications are also likely that include gastrointestinal bleeding from gastric antral vascular ectasia, erosions or ulcers. Incidence of gastrointestinal disorders is considered to increase with the duration of renal failure, independent of dialysis modality. While uremia and dialysis have been linked to an increased risk of gastrointestinal tract lesions, pathogenesis of gastrointestinal dysfunction in end-stage renal disease is considered to be multifactorial and has not yet been clarified. In addition, conflicting data exist on the association of renal dysfunction with gastrointestinal disorders, and there are no explicit guidelines for the management of co-morbid gastrointestinal problems in patients with concomitant renal failure. Herein, we review the common upper gastrointestinal disorders that occur among dialysis patients, with an emphasis on prevalence, pathogenesis and diagnostic strategies.

Keywords: End-stage renal disease, peritoneal dialysis, hemodialysis, upper gastrointestinal tract, pathogenesis

DİYALİZ HASTALARINDA ÜST GASTROİNTESTİNAL SİSTEM HASTALIKLARI

ÖZET

Diyaliz hastalarında komorbid gastrointestinal semptomlar yüksek prevalansa sahiptir. Bulantı, kusma ve mide yanması gibi dispeptik semptomlar en yaygın gastrointestinal semptomlardır. Üst gastrointestinal sistem hastalıkları (örn., peptic ülser hastalığı ve gastroparezi) bu semptomların önemli nedenleri arasındadır. Ek olarak gastrik antral vasküler ektaziye bağlı kanama erozyon veya ülser gelişimi gibi nadir ancak şiddetli komplikasyonlar da gözlenebilmektedir. Gastrointestinal hastalık insidansının, diyaliz türünden bağımsız ve renal yetmezlik süresi ile orantılı olarak artış gösterdiği kabul edilmektedir. Üremi ve diyaliz gastrointestinal sistem lezyon gelişimi için bir risk faktörü olmakla birlikte, son dönem renal hastalığa bağlı gastrointestinal fonksiyon bozukluğu gelişimi çok faktörlü ve henüz netlik kazanmamış bir patogeneze sahiptir. Ek olarak, renal fonksiyon bozukluğu ve gastrointestinal bozukluklar arasındaki ilişkiye dair çelişkili veriler mevcut olup, renal yetmezlik zemininde gelişen gastrointestinal hastalıkların yönetimine dair özgül kılavuzlar bulunmamaktadır. Bu derleme makalede, diyaliz hastalarında sık gözlenen üst gastrointestinal sistem hastalıkları prevalans, patogenez ve tanısal yaklaşımlar bazında sunulmaktadır.

Anahtar sözcükler: Son dönem renal hastalık, periton diyalizi, hemodiyaliz, üst gastrointestinal sistem, patogenez

Gastrointestinal diseases represent the most common, non-renal, chronic disorders that accompany end-stage renal disease (ESRD) (1,2). ESRD has been associated with a high prevalence, from 70% to 79%, of co-morbid gastrointestinal symptoms, which appear to be independent of dialysis modality, while the incidence of these GI disorders increases with the duration of renal failure (2-4). The

most common gastrointestinal symptoms in dialysis patients include dyspeptic symptoms, such as nausea, vomiting, and epigastric burning (2,4-8). Less common but severe complications include gastrointestinal bleeding from gastric antral vascular ectasia, erosions or ulcers (8).

Underlying these symptoms is a wide(broad) spectrum of gastrointestinal diseases that include the upper gastrointestinal (UGI) tract [e.g., peptic ulcer disease (PUD) and gastroparesis], the lower gastrointestinal (LGI) tract (e.g., diverticular disease, angiodysplasia, mesenteric ischemia, ischemic colitis, colonic perforation, fecal impaction and stercoral ulcer, dialysis-related amyloidosis, encapsulating peritoneal sclerosis, and idiopathic dialysis ascites], and the accessory digestive glands (e.g., cholecystitis, cholecystolithiasis, hepatitis, and pancreatitis) (7,9).

A great number of gastrointestinal complications have been reported to accompany renal failure based on the interrelationship of gastrointestinal and renal diseases (8) (Table 1).

While uremia and dialysis have been linked to an increased risk of gastrointestinal tract lesions, pathogenesis of gastrointestinal dysfunction in ESRD is considered (as a) or (to be) multifactorial with the contribution of several factors (2,5,8,10), including gastric hypomotility with delayed gastric emptying (8), capillary fragility and disordered hemostasis of uremia (8), effects of unfiltered humoral factors or toxins (6), hypergastrinemia (11), reduced visceral sensitivity (12), comorbidities (8), and medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) (8,13). In addition, conflicting data exist on the association between renal dysfunction and gastrointestinal disorders with no explicit guidelines for the management of co-morbid gastrointestinal problems in renal failure (2,10).

This review focused on UGI disorders among dialysis patients, the LGI disorders and diseases of accessory digestive glands were not within the scope of the present review. We, therefore, examined the common UGI disorders that occur among dialysis patients with an emphasis on prevalence, pathogenesis and diagnostic strategies.

Upper gastrointestinal disorders

Dyspepsia is a set of symptoms suggestive of a reflux, ulcer or motility disorder, while associated with increased likelihood of gastrointestinal complications such as UGI hemorrhage, disturbed quality of life and poor outcome of kidney disease (2,7,14).

Table 1. Interrelationship of gastrointestinal and renal diseases[8]

Gastrointestinal Manifestations of Renal Disease
Acute renal failure
Gastric and duodenal erosions
Gastric perforation
Chronic renal failure
Erosive esophagitis
Erosive and hemorrhagic gastritis
(Nodular) duodenitis
Peptic ulcer disease
Angiodysplasia
Intussusception secondary to mucosal hemorrhage
Diverticula in adult polycystic kidney disease (APCKD)
Salmonella enteritis
Calcific uremic arteriolopathy
Complications of therapy
Kayexalate sorbitol associated GI mucosal injury
Anticoagulant and antiplatelet therapy associated GI bleeding
Mycophenylate mofetil associated GI mucosal injury(transplants)
Complications of dialysis
Acute fluid loss resulting in nonocclusive intestinal ischemia
Peritonitis (bacterial or chemical) in peritoneal dialysis
Hernia (+/− obstruction or incarceration) in peritoneal dialysis
Sclerosing peritonitis in long-term peritoneal dialysis
Renal transplantation
Gastric and duodenal erosions and ulcers
Esophagitis (often candida)
Mycophenylate mofetil associated GI mucosal injury
Perforation of colonic diverticula (especially APCKD)
Cecal ulceration
Pseudomembranous colitis (50% of patients receiving antibiotics)
Nonocclusive vascular insufficiency
Infections due to chronic immunosupression, especially
cytomegalovirus infection and intestinal strongyloidiasis
Posttransplant GI lymphoproliferative disorders
Diseases Affecting Both Gastrointestinal and Renal Systems
Collagen vascular diseases (scleroderma, vasculitides)
Diabetes mellitus
Hyperparathyroidism
Amyloidosis
Myeloma
Henoch–Schonlein purpura
Hemolytic uremic syndrome
Renal Manifestations of Gastrointestinal Disease
Crohn's disease
Calcium oxalate stones
Ureteral obstruction
Entero or colovesical fistula
Perinephric abscess

Adapted from "Riddell R, Jain D. Gastrointestinal Manifestations of Extraintestinal Disorders and Systemic Disease. Chapter 8. In: Lewin, Weinstein, and Riddell's Gastrointestinal Pathology and Its Clinical Implications. Wloters Kluwer, UK, 2014, pp. 390-393. Available at: http://www.lww.co.uk/media/Riddell-Ch8-Gastrointestinal-Manifestations-of-Extraintestinal-Disorders-and-Systematic-Disease.pdf

The prevalence of dyspepsia among ESRD patients on hemodialysis ranges from 48% to 70% that exceeds the rates (40%) in the general population (5,15). High prevalence of dyspeptic symptoms such as nausea, vomiting, epigastric burning and postprandial fullness in patients with renal failure formed the basis of investigations addressing the prevalence of underlying UGI lesions in these patients (7,14).

However, while studies prior to the common use of esophagogastroduodenoscopy (EGD) indicated a higher prevalence of gastric and duodenal ulcers in patients with renal failure compared to the general population (2), later EGD-based studies confirmed a higher prevalence of UGI erosions and inflammation in renal failure but revealed conflicting data on the prevalence of ulcerations (4,16-18). In an endoscopic study, the peptic ulceration was reported to be evident only in 2% of renal failure patients, which was similar to the rates observed in the general population (17).

Studies in uremic patients on maintenance hemodialysis also revealed conflicting data with increased prevalence of gastroduodenal lesions (e.g., gastritis, duodenitis, and peptic ulcers) reported in some studies, whereas the prevalence was found to be similar to the general population in others (6,8). Notably, neither the severity of renal dysfunction nor the duration of hemodialysis was shown to be correlated with the prevalence of gastrointestinal lesions in patients with chronic renal failure (8,19).

In another endoscopic study among dyspeptic patients, the prevalence of peptic lesions and Helicobacter pylori (H. pylori) infection was reported to be 74% and 52%, respectively, in patients with renal failure, while 18% and 36%, respectively, in patients with normal renal function (18). Authors also noted low symptoms scores in uremic patients despite the presence of H. pylori infection (18).

Differences between studies in terms of patient populations, comorbid disorders, sample sizes, investigative techniques, the prevalence of H. pylori infection and the use of NSAID agents have been considered likely to be associated with the occurrence of conflicting results (8). Nonetheless, it should also be noted that dyspepsia is a set of symptoms associated with various conditions ranging from normal functional dyspepsia to organic dyspepsia secondary to gastrointestinal diseases, such as peptic ulcers and cancer (18). Common causes of organic dyspepsia are listed in Table 2 (7).

Table 2. Differential diagnosis of organic dysypepsia[7]

- Peptic ulcer disease
- Gastroesophageal reflux disease (GERD)
- Biliary pain
- Chronic abdominal wall pain
- Gastric or esophageal cancer
- Gastroparesis
- Pancreatitis
- Carbohydrate malabsorption
- Medications (including potassium supplements, digitalis, iron, theophylline, oral antibiotics [especially ampillin and erythromycin], NSAIDs, corticosteroids, niacin, gemfibrozil, narcotics, colchicine, quinidine, estrogens, levodopa)
- Infiltrative diseases of the stomach (eg, Crohn's disease sarcoidosis)
- Metabolic disturbances (hypercalcemia, hyperkalemia)
- Hepatoma
- Ischemic bowel disease
- Systemic disorders (diabetes mellitus, thyroid and parathyroid disorders, connective tissue disease)
- Intestinal parasites (Giardia, Strongyloides)
- Abdominal cancer, especially pancreatic cancer

Adapted from "Barri YM, Golper TA. Gastrointestinal disease in dialysis patients. 2016. Available at http://www.uptodate.com/contents/gastrointestinal-disease-in-dialysis-patients"

Peptic ulcer disease

Although previous studies have suggested a higher incidence of ESRD in patients on dialysis and that of PUD in patients with or without CKD (7,9,20), later on, endoscopic studies showed that PUD was no more frequent in dialysis than in non-dialysis patients (7,9). However, in an EGD study of 299 patients on dialysis and 400 healthy controls, the dialysis population had higher rates of gastritis (77.8% vs. 46.8%), gastric ulcers (11.4% vs. 4.1%) and duodenal ulcers (6.4% vs. 3.3%) (21).

Hence, while incidence of bleeding from PUD was shown to be high in CKD patients, an ongoing debate exists whether the incidence of PUD itself is high in uremic patients when compared to the general population (7,9).

PUD diagnosis in dialysis patients

The first steps in the management of PUD are to assess H. pylori infection status and to administer NSAIDs therapy (7). Given the association of a high prevalence of UGI symptoms, UGI lesions, and H. pylori infection with renal failure, it has been suggested that all patients with renal failure and dyspepsia should be assessed for H. pylori infection and treated if positive (2,16). However, no correlation of dyspeptic symptoms seems to exist with either H. pylori infection or gastrointestinal lesions in renal failure patients (2,18,22). Moreover, noninvasive tests, such as

serology tests and the urea breath test, are considered less sensitive and specific in cases of renal failure when compared to patients with normal renal function (23,24).

According to the American Gastroenterological Association position statement, the use of EGD is recommended in the evaluation of H. pylori infections in renal failure patients if there is a new-onset dyspepsia without evidence of gastroesophageal reflux disease (GERD) or NSAID use, and in cases of alarming symptoms, such as weight loss, progressive dysphagia or recurrent vomiting, evidence of gastrointestinal bleeding, or a family history of cancer (25).

PUD risk factors in dialysis patients (NSAIDS vs. H. pylori)

H. pylori infection and the use of NSAIDs are the two major risk factors associated with PUD with similar significance in dialysis and non-dialysis patients (7,9,26).

A similar incidence of H. pylori infection in patients on regular dialysis when compared to other populations was reported in several studies (4,23,24). However, some studies have reported a higher prevalence of H. pylori infection in renal failure patients than in the general population (16,18), and still others have reported even lower rates of H. pylori infection in uremic patients (21,27), particularly those on hemodialysis (7,28). In another study, lower dyspeptic symptom scores but a higher prevalence of peptic lesions was shown in uremic patients when compared to patients with normal renal function, irrespective of H. pylori infection (18).

The reported prevalence of H. pylori infection in patients with uremia varies from 21% to 73% (16,17,19,23,29) but does not exceed that of the general population (6,8,27). According to a recent consensus, the prevalence of H. pylori infection in chronic renal failure patients receiving peritoneal or hemodialysis is considered to be equal or lower when compared with the subjects with normal renal function in various different geographic populations, regardless of the presence of gastric symptoms (10,21,30).

Suppression of H. pylori growth via elevated urea levels and increased gastric pH due to elevated inflammatory cytokines and the likelihood of partial treatment of H. pylori via commonly used antibiotics in the dialysis population are suggested to contribute to the lower prevalence of H. pylori observed in dialysis patients (9,21).

However, the prevalence of PUD was reported to be higher in dialysis patients with H. pylori infection when compared with dialysis patients without H. pylori infection (21,23) and to individuals with normal renal function (16).

Some studies revealed no association between H. pylori positivity and the prevalence or intensity of dyspeptic symptoms (18,31) or delayed gastric emptying (31) in uremic patients, irrespective of dialysis therapy (18,31). However, this association was closely related to gastroduodenal peptic lesions in dyspeptic patients with normal renal function (18).

Upper gastrointestinal bleeding

UGI bleeding from gastritis, duodenitis, peptic ulcers, and telangiectasia is more common in ESRD patients, particularly those on hemodialysis, when compared to the general population. In ESRD patients, the estimated frequency is 21 bleeds per 1,000 patient years with a very high risk of mortality accounting for 3–7% of all deaths (7,8,32,33). Disordered hemostasis of uremia resulting from platelet and endothelial dysfunction, associated anemia, secondary hyperparathyroidism and the use of medications that likely affect the clotting cascade (e.g., clopidogrel, aspirin, and other NSAIDs) are considered risk factors for UGI bleeding (2,9,32,34).

The prognosis of UGI bleeding in ESRD patients is generally worse than in the normal population, and renal insufficiency is considered one of the predictors of mortality in validated UGI bleeding scores alongside age, the presence of shock and other comorbidities (9,35).

Causes of UGI bleeding

Among ESRD patients, the duodenum is considered to be the most common site of UGI bleeding (36), while angiodysplasia and gastrointestinal tract erosions refer to the most common causes underlying UGI bleeding (2,7,37,38). Higher rate of angiodysplasia was shown in patients on hemodialysis than in those on peritoneal dialysis (7). Gastric antral vascular ectasia was documented as the most common cause of UGI bleeding as well as recurrent bleeding in patients who received dialysis therapy during emergencies, followed by gastroduodenal ulcer disease (34,39).

However, angiodysplasia has also been indicated to occur at a much lower incidence when considered as a cause of UGI bleeding in patients with ESRD, with incidence similar to the general population (7). No difference was noted in the causes and outcomes of UGI bleeding in patients with (n=40) and without (n=30) chronic renal failure in a retrospective study (39). Therefore, it remains unclear whether angiodysplasia or vascular ectasia has a higher prevalence in uremic patients than in the general population (6-8).

In a larger study of 727 patients with UGI bleeding who underwent diagnostic endoscopy, angiodysplasia was shown to be a more frequent cause of UGI bleeding (13% vs. 1.3%) in patients with renal dysfunction, while gastric ulcer (37%) and duodenal ulcer (23%) were more common causes of bleeding when compared to angiodysplasia in cases of renal failure (37). PUD appears to be the most common cause of UGI bleeding in patients with renal failure (7). Although angiodysplasia may currently be a less frequent cause of UGI bleeding than previously reported (7), it seems to be a more common source of bleeding in patients with more severe and prolonged renal disease (37).

Other than PUD and angiodysplasia, causes of UGI bleeding among uremic patients include esophageal varices, Mallory–Weiss tears, tumors, esophagitis, and Dieulafoy's lesions (9,40).

Diagnosis of UGI bleeding

A higher incidence of gastrointestinal bleeding in the CKD population emphasizes the importance of prompt recognition (9). The value of anemia as well as iron deficiency as a diagnostic sign of gastrointestinal bleeding is limited in patients who are receiving dialysis, while patients with overt gastrointestinal blood loss, rapidly changing hemoglobin levels and a failure to restore iron stores in spite of adequate replacement should undergo further evaluation, including endoscopy (9).

Risk of recurrent bleeding

Conflicting data exist concerning the risk of recurrent bleeding in patients with ESRD. Although several studies have reported a higher rate of recurrence of gastrointestinal bleeding in patients with ESRD when compared to those without renal disease as well as when compared to patients with CKD (41), other studies reported a lack of such an increased risk (7,9,40).

Gastroparesis

Motility disorders, such as delayed emptying or gastroparesis, may be associated with uremia, thereby leading to anorexia, nausea, and vomiting. Gastroparesis is a frequent indication to initiate dialysis and usually resolves after the onset of renal replacement therapy (7).

Data from small-scale studies among renal failure patients revealed inconclusive data on gastric emptying in CKD patients; some noted no difference in gastric emptying in CKD patients when compared to healthy controls (42), while some others indicated a prolonged gastric emptying in CKD patients (43) but not in hemodialysis patients (43,44) when compared to controls (43).

Gastroparesis that is unresponsive to dialysis is sometimes caused by an autonomic neuropathy, particularly if the gastroparesis results from co-morbid diabetes (43,45,46). An overall higher prevalence of gastrointestinal symptoms was reported when renal failure was associated with diabetes rather than other etiologies (3,47). Diabetes mellitus itself has also been considered likely to perpetuate gastroparesis and its resulting symptoms (45). However, gastroparesis is suggested to commonly occur in the absence of diabetes (2,46,47).

Delayed gastric emptying has been reported to occur in as many as 36% of patients with renal failure (48) and has been associated with a high prevalence of dysmotility (46) as well as malnutrition in some patients with ESRD (7).

Delayed gastric emptying was reported in peritoneal dialysis patients (49,50), independent of diabetic status and without associated gastrointestinal symptoms such as nausea and vomiting with gastroparesis (50). In a prospective assessment of gastric emptying in 53 nondiabetic patients (26 on hemodialysis and 27 controls), gastric emptying was shown to be significantly longer in dyspeptic patients on hemodialysis than in healthy controls and in dyspeptic patients on hemodialysis when compared to non-dyspeptic patients on hemodialysis (46).

Nonetheless, the exact pathogenesis of gastroparesis remains unclear in renal failure patients (2).

Conclusion

In conclusion, this review has summarized common UGI disorders among dialysis patients with an emphasis upon prevalence, pathogenesis and diagnostic strategies.

Although recent EGD-based studies have confirmed a higher prevalence of UGI erosions and inflammation in patients with renal failure when compared to the general population (4,16,18), *conflicting data on gastric and duodenal ulcers with no evidence on a definite increase in the prevalence of ulcerations in renal failure* (4,16-18).(**I think this sentence needs a verb?!)

Recent consensus showed that the prevalence of H. pylori infection in dialysis patients was equal or lower when compared to subjects with normal renal function in various different geographic populations, regardless of the presence of gastric symptoms (10,21,30). However, the prevalence of PUD was reported to be higher in dialysis patients with H. pylori infection when compared to

dialysis patients without H. pylori infection (21) and when compared to individuals with normal renal function (16). Nonetheless, PUD appears to be the most common cause of UGI bleeding (7), while gastroparesis commonly occurs among uremic patients in the absence of diabetes, regardless of dialysis modality (2,46,47).

This review emphasizes the differentiation and careful consideration of gastrointestinal symptoms and associated gastrointestinal diseases in dialysis patients, given these patients' high prevalence and association with poor clinical outcomes if not recognized and managed properly. Given the lack of specific guidelines that formulate appropriate screening and treatment plans, as well as inconclusive data on the prevalence and management of gastrointestinal diseases among dialysis patients, further investigation seems necessary to address the diagnostic models, practice patterns and prognostic characteristics with respect to dialysis modality in large-scale ESRD populations.

Author Contributions
Kiziltas S and Sahin S performed conception and design of the paper and drafting and revising the article, Kiziltas S had primary responsibility for final content.

Conflict of Interest
No conflict of interest was declared by the authors.

Financial Disclosure
No financial disclosure was received.

References

1. Nespor SL, Holley JL. Patients on hemodialysis rely on nephrologists and dialysis units for maintenance health care. ASAIO J 1992;38:M279-81.
2. Shirazian S, Radhakrishnan J. Gastrointestinal disorders and renal failure: exploring the connection. Nat Rev Nephrol 2010; 6: 480-92. [CrossRef]
3. Strid H, Simrén M, Johansson AC, Svedlund J, Samuelsson O, Björnsson ES. The prevalence of gastrointestinal symptoms in patients with chronic renal failure is increased and associated with impaired psychological general well-being. Nephrol Dial Transplant 2002;17:1434-9.
4. Abu Farsakh NA, Roweily E, Rababaa M, Butchoun R. Brief report: evaluation of the upper gastrointestinal tract in uraemic patients undergoing haemodialysis. Nephrol Dial Transplant 1996;11:847-50.
5. Chong VH, Tan J. Prevalence of gastrointestinal and psychosomatic symptoms among Asian patients undergoing regular hemodialysis. Nephrology (Carlton) 2013; 18: 97-103. [CrossRef]
6. Etemad B. Gastrointestinal complications of renal failure. Gastroenterol Clin North Am 1998; 27: 875-92.
7. Barri YM, Golper TA. Gastrointestinal disease in dialysis patients. 2016. Available at: http://www.uptodate.com/contents/gastrointestinal-disease-in-dialysis-patients. Accessed on: March 26, 2019
8. Riddell R, Jain D. Gastrointestinal Manifestations of Extraintestinal Disorders and Systemic Disease. Chapter 8. In: Lewin, Weinstein, and Riddell's Gastrointestinal Pathology and Its Clinical Implications. Wloters Kluwer; UK, 2014, pp. 390-3. Available at: http://www.lww.co.uk/media/Riddell-Ch8-Gastrointestinal-Manifestations-of-Extraintestinal-Disorders-and-Systematic-Disease.pdf
9. Kalman RS, Pedrosa MC. Evidence-based review of gastrointestinal bleeding in the chronic kidney disease patient. Semin Dial 2015;28:68-74. [CrossRef]
10. Thomas R, Panackal C, John M, et al. Gastrointestinal complications in patients with chronic kidney disease. A 5-year retrospective study from a tertiary referral center. Ren Fail 2013; 35: 49-55. [CrossRef]
11. Muto S, Murayama N, Asano Y, Hosoda S, Miyata M. Hypergastrinemia and achlorhydria in chronic renal failure. Nephron 1985; 40: 143-8. [CrossRef]
12. Laaksonen S, Voipio-Pulkki L, Erkinjuntti M, Asola M, Falck B. Does dialysis therapy improve autonomic and peripheral nervous system abnormalities in chronic uraemia? J Intern Med 2000; 248: 21-6.
13. Lee YC, Hung SY, Wang HH, Wang HK, Lin CW, Chang MY et al. Different Risk of Common Gastrointestinal Disease Between Groups Undergoing Hemodialysis or Peritoneal Dialysis or With Non-End Stage Renal Disease: A Nationwide Population-Based Cohort Study. Medicine (Baltimore) 2015; 94: e1482. [CrossRef]
14. Hammer J, Oesterreicher C, Hammer K, Koch U, Traindl O, Kovarik J. Chronic gastrointestinal symptoms in hemodialysis patients. Wien Klin Wochenschr 1998; 110:287-91.
15. Santos PR, Monteiro DL, de Paula PH, et al. Volaemic status and dyspepsia in end-stage renal disease patients. Nephrology (Carlton) 2015; 20: 519-22. [CrossRef]
16. Khedmat H, Ahmadzad-Asl M, Amini M, et al. Gastro-duodenal lesions and Helicobacter pylori infection in uremic patients and renal transplant recipients. Transplant Proc 2007; 39: 1003-7. [CrossRef]
17. Kang JY, Ho KY, Yeoh KG, et al. Peptic ulcer and gastritis in uraemia, with particular reference to the effect of Helicobacter pylori infection. J Gastroenterol Hepatol 1999; 14: 771-8.
18. Nardone G, Rocco A, Fiorillo M, et al. Gastroduodenal lesions and Helicobacter pylori infection in dyspeptic patients with and without chronic renal failure. Helicobacter 2005; 10: 53-8. [CrossRef]
19. Stolic RV, Jovanovic AN, Zivic ZP, et al. Influence of the level of renal insufficiency on endoscopic changes in the upper gastrointestinal tract. Am J Med Sci 2008; 336: 39-43. [CrossRef]
20. Bacci MR, Chehter EZ. Dyspepsia among patients with chronic kidney disease: a cross sectional study. Int Arch Med 2013; 6: 43. [CrossRef]
21. Sugimoto M, Sakai K, Kita M, Imanishi J, Yamaoka Y. Prevalence of Helicobacter pylori infection in long-term hemodialysis patients. Kidney Int 2009; 75: 96-103. [CrossRef]
22. Luzza F, Imeneo M, Maletta M, et al. Helicobacter pylori-specific IgG in chronic haemodialysis patients: relationship of hypergastrinaemia to positive serology. Nephrol Dial Transplant 1996; 11: 120-4.
23. Huang JJ, Huang CJ, Ruaan MK, Chen KW, Yen TS, Sheu BS. Diagnostic efficacy of (13)C-urea breath test for Helicobacter pylori infection in hemodialysis patients. Am J Kidney Dis 2000; 36: 124-9. [CrossRef]
24. Wang YL, Sheu BS, Huang JJ, Yang HB. Noninvasive stool antigen assay can effectively screen Helicobacter pylori Infection and assess success of eradication therapy in hemodialysis patients. Am J Kidney Dis 2001; 38: 98-103. [CrossRef]
25. Talley NJ, American Gastroenterological Association medical position statement: evaluation of dyspepsia. Gastroenterology 2005; 129: 1753-5. [CrossRef]

26. Sheu BS, Huang JJ. Helicobacter pylori infection in hemodialysis patients. Int J Artif Organs 2001; 24: 669-70.
27. Chang SS, Hu HY. Lower Helicobacter pylori infection rate in chronic kidney disease and end-stage renal disease patients with peptic ulcer disease. J Chin Med Assoc 2014; 77: 354-9. [CrossRef]
28. Nakajima F, Sakaguchi M, Amemoto K, et al. Helicobacter pylori in patients receiving long-term dialysis. Am J Nephrol 2002; 22: 468-72. [CrossRef]
29. Cocchiara G, Romano M, Buscemi G, Maione C, Maniaci S, Romano G. Advantage of eradication therapy for Helicobacter pylori before kidney transplantation in uremic patients. Transplant Proc 2007; 39: 3041-3. [CrossRef]
30. Sugimoto M, Yamaoka Y. Review of Helicobacter pylori infection and chronic renal failure. Ther Apher Dial 2011; 15: 1-9. [CrossRef]
31. Schoonjans R, Van VB, Vandamme W, et al. Dyspepsia and gastroparesis in chronic renal failure: the role of Helicobacter pylori. Clin Nephrol 2002; 57: 201-7.
32. Sohal AS, Gangji AS, Crowther MA, Treleaven D. Uremic bleeding: pathophysiology and clinical risk factors. Thromb Res 2006;118: 417-22. [CrossRef]
33. Wasse H, Gillen DL, Ball AM, et al. Risk factors for upper gastrointestinal bleeding among end-stage renal disease patients. Kidney Int 2003;64: 1455-61. [CrossRef]
34. Ikeda N, Inoue T, Kobayashi K, Watanabe Y, Suzuki H. Emergency gastrointestinal bleeding in dialysis patients five years' experience in a single dialysis center. Urol Nephrol Open Access J 2015; 2: 00021. [CrossRef]
35. Rockall TA, Logan RF, Devlin HB, Northfield TC. Risk assessment after acute upper gastrointestinal haemorrhage. Gut 1996; 38: 316-21.
36. Akmal M, Sawelson S, Karubian F, Gadallah M. The prevalence and significance of occult blood loss in patients with predialysis advanced chronic renal failure (CRF), or receiving dialytic therapy. Clin Nephrol 1994; 42: 198-202.
37. Chalasani N, Cotsonis G, Wilcox CM. Upper gastrointestinal bleeding in patients with chronic renal failure: role of vascular ectasia. Am J Gastroenterol 1996; 91: 2329-32.
38. Poralla T. Angiodysplasia in the renal patient: how to diagnose and how to treat? Nephrol Dial Transplant 1998; 13: 2188-91.
39. Alvarez L, Puleo J, Balint JA. Investigation of gastrointestinal bleeding in patients with end stage renal disease. Am J Gastroenterol 1993;88:30-3.
40. Zuckerman GR, Cornette GL, Clouse RE, Harter HR. Upper gastrointestinal bleeding in patients with chronic renal failure. Ann Intern Med 1985; 102: 588-92.
41. Cheung J, Yu A, LaBossiere J, Zhu Q, Fedorak RN. Peptic ulcer bleeding outcomes adversely affected by end-stage renal disease. Gastrointest Endosc 2010; 71: 44-9. [CrossRef]
42. Freeman JG, Cobden I, Heaton A, Keir M. Gastric emptying in chronic renal failure. Br Med J (Clin Res Ed) 1985; 291:1048.
43. McNamee PT, Moore GW, McGeown MG, Doherty CC, Collins BJ. Gastric emptying in chronic renal failure. Br Med J (Clin Res Ed) 1985;291:310-1.
44. Soffer EE, Geva B, Helman C, Avni Y, Bar-Meir. Gastric emptying in chronic renal failure patients on hemodialysis. J Clin Gastroenterol 1987; 9: 651-3.
45. Drossman DA, Li Z, Andruzzi E, et al. U.S. householder survey of functional gastrointestinal disorders. Prevalence, sociodemography, and health impact. Dig Dis Sci 1993; 38: 1569-80.
46. Van Vlem B, Schoonjans R, Vanholder R, et al. Delayed gastric emptying in dyspeptic chronic hemodialysis patients. Am J Kidney Dis 2000; 36: 962-8.
47. Bytzer P, Talley NJ, Leemon M, Young LJ, Jones MP, Horowitz M. Prevalence of gastrointestinal symptoms associated with diabetes mellitus: a population-based survey of 15,000 adults. Arch Intern Med 2001; 161: 1989-96.
48. Strid H, Simrén M, Stotzer PO, Abrahamsson H, Björnsson ES. Delay in gastric emptying in patients with chronic renal failure. Scand J Gastroenterol 2004; 39: 516-20.
49. Brown-Cartwright D, Smith HJ, Feldman M. Gastric emptying of an indigestible solid in patients with end-stage renal disease on continuous ambulatory peritoneal dialysis. Gastroenterology 1988;95:49-51.
50. Bird NJ, Streather CP, O'Doherty MJ, Barton IK, Gaunt JI, Nunan TO. Gastric emptying in patients with chronic renal failure on continuous ambulatory peritoneal dialysis. Nephrol Dial Transplant 1994;9:287-90.