

# Mesenteric ischemia in hemodialysis patients

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## SUMMARY

**Introduction:** Mesenteric ischaemia is an abdominal pathology with a high mortality rate. Among the population under dialysis treatment it presents some different traits such as non-occlusive mesenteric attacks in most of the cases. Its diagnosis is difficult and it is usually the result of an interdisciplinary collaboration. It is necessary to know better the symptoms of this illness among dialytic patients in order to improve its prognosis. **Patients and methods:** Eleven haemodialytic patients in our hospital (0.87% per patient-year) have diagnosed with mesenteric ischaemia confirmed by a laparotomy. We will list the main risk factors of this pathology, its symptoms, its evolution, some radiological and laboratory data more pointed out, the surgical findings and its treatment. **Results:** Ten patients (91%) had suffer from cardiovascular pathologies, five of them (45%) had suffer an ischaemia cardiopathy. Seven patients (64%) had a spell of arterial hypotension during their haemodialysis session, which preceded mesenteric ischaemia. The reason for consulting a physician was abdominal pain, specially on the right hemiabdomen (64%). The analytical date most frequently observed was leucocytosis (54%). The usual radiological tests such as abdominal plain radiography and ecography didn't give any detailed formation. Ten out of eleven patients (91%) had necrosis on the intestinal wall. The ileum was the most affected intestinal section. Five of the patients presented only a limited damage of the ileum (45%). Two patients (18%) presented an extensive damage in the whole small intestine and part of the right colon. Intestinal resection was the most chosen way of treatment, which was practiced on eight patients (73%). Only three of them (27%) survived the mesenteric ischaemia and were sent to their homes. The key factor of their survival was that they were operated on in less than 8 hours from their arrival at emergency room. **Conclusions:** Mesenteric ischaemia must be expected among patients under haemodialysis who suffer from abdominal pain, especially if they have had some arterial hypotensive spells during their previous dialytic session. It's a matter of urgent surgery where not only its diagnosis but also its early surgical treatment can lessen its high morbi-mortality risk.

**Key words:** Haemodialysis. Mesenteric ischaemia. Risk factors. Treatment.

## RESUMEN

**Introducción:** La isquemia mesentérica es una patología abdominal con una elevada mortalidad. En la población en diálisis presenta unas características diferentes como la existencia en la mayoría de casos de infarto mesentérico no trombótico. Su diagnóstico resulta difícil y suele ser interdisciplinar. Es necesario conocer mejor las características de esta enfermedad en los pacientes en diálisis para intentar mejorar su pronóstico. **Pacientes y métodos:** Once pacientes en hemodiálisis de nuestro hospital (0,87% por paciente-año) han sido diagnosticados de isquemia mesentérica confirmada por laparotomía. Describimos los principales factores de riesgo para padecer esta patología, la evolución, la clínica, los datos radiológicos y de laboratorio más destacados, los hallazgos quirúrgicos y su tratamiento. **Resultados:** Diez pacientes (91%) tenían antecedentes de patología cardiovascular, cinco de ellos (45%) cardiopatía isquémica. Un episodio de hipotensión arterial durante la sesión de hemodiálisis que precedió a la isquemia mesentérica, tuvo lugar en siete enfermos (64%). El dolor abdominal fue el motivo de consulta en diez casos (91%), localizándose de manera más frecuente (64%) en hemiabdomen derecho. La leucocitosis fue el dato analítico más frecuentemente observado (54%). Las pruebas radiológicas convencionales como la radiografía simple de abdomen y la ecografía abdominal no aportaron información específica. Diez de los once pacientes (91%) presentaban necrosis de la pared intestinal. El íleon fue el tramo intestinal más afectado, de manera limitada en 5 casos (45%) y de forma masiva al existir afectación de todo el intestino delgado y gran parte del colon derecho, en dos enfermos (18%). La resección intestinal fue el tratamiento de elección, practicándose en ocho enfermos (73%). Sólo tres pacientes (27%) sobrevivieron a la isquemia mesentérica, pudiendo ser alta hospitalaria. En ellos la intervención quirúrgica fue temprana en menos de 8 horas desde su llegada a urgencias. **Conclusiones:** La isquemia mesentérica debe sospecharse en los pacientes en hemodiálisis que presenten dolor abdominal más si han presentado algún episodio de hipotensión arterial en la sesión previa de diálisis. Se trata de una urgencia quirúrgica, en la que tanto el diagnóstico como el tratamiento quirúrgico precoz pueden disminuir su elevada morbi-mortalidad.

**Palabras clave:** Hemodiálisis. Isquemia mesentérica. Factores de riesgo. Tratamiento.

## INTRODUCTION

Mesenteric ischemia is a rare pathology among the general population, with an incidence of 0.09%-0.2% per patient/year.<sup>1,2</sup> In these patients it predominantly has an occlu-

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**Table I. Most relevant previous pathological conditions**

Arterial hypertension	4 (36%)
Diabetes Mellitus	2 (18%)
Coronary heart disease	5 (45%)
Peripheral vascular disease	2 (18%)
Cerebrovascular accident	2 (18%)
Atrial fibrillation	1 (9%)
Central retinal vein thrombosis	1 (9%)
Heart failure	1 (9%)
Obstructive pulmonary disease	1 (9%)
Neoplasm of the colon	2 (18%)
Previous renal transplant	1 (9%)

sive origin due to thrombosis formation on preexistent atherosclerotic lesions.<sup>3</sup> In the dialysis population it is more common, with reported incidence rates up to 1.9% per patient/year.<sup>4</sup> In these patients, the ischemic condition may involve the small bowel and/or the colon, and it usually is non-occlusive. Events compromising the mesenteric blood flow upon an already altered circulation due to atherosclerosis-induced stenotic lesions may precipitate the development of mesenteric ischemia. The precipitating factors may be fast and excessive ultrafiltration during the dialysis sessions with the resulting arterial hypotension, or volume depletion due to other causes independent of dialysis such as diarrhea, vomiting, fever or acute states of low cardiac output.<sup>3,5,6</sup> Mesenteric ischemia is a condition with high mortality, even higher among dialysis patients that more frequently have an altered right colon, which is in itself associated to a poorer prognosis and that adds to the high risk and prevalence of cardiovascular pathology they present.<sup>7,8</sup>

The aim of the present study is to describe the cases with mesenteric ischemia diagnosed for the last 19 years among hemodialysis patients at our Center as well as better knowing this condition, which would allow us for an earlier diagnosis and improved prognosis.

## PATIENTS AND METHODS

We have included in this study all hemodialysis patients presenting with mesenteric ischemia, confirmed at surgery, from January of 1988 to January of 2007. The patients were on a chronic dialysis program at our Hospital. In each one of the eleven patients we analyzed the clinical picture they presented in relation to mesenteric ischemia, the more relevant pathologies in their personal histories, and the laboratory and radiological findings at the time of diagnosis. From a surgical perspective, we report on the intestinal areas involved and the treatment performed. We describe the post-surgical course and the cause of death. We reviewed the literature regarding this abdominal condition and the differences found between patients submitted or not to dialysis

## RESULTS

During the last 19 years, an average of 66.41 (33-90) patients per year have received dialysis at our Hospital, the presence

**Table II. Most relevant initial clinical and laboratory data**

Abdominal pain	10 (91%)
Arterial hypotension episode during previous HD	7 (64%)
Leukocytosis (> 10,000/mm <sup>3</sup> )	6 (54%)
Abdominal defense	6 (54%)
Vomiting	5 (45%)
Hb decrease > 10%	4 (36%)
Diarrheas	3 (27%)
Shock (Máx. BP < 100 mmHg)	3 (27%)
Fever (> 37.5 °C)	0 (0%)

of mesenteric ischemia being surgically confirmed in 11 of them.

They were 7 males (64%) and 4 females (36%), with a mean age of 71 years (58-79). The most relevant preexisting pathological conditions are shown in table I. Eleven patients (91%) had previously had some episode of cardiovascular pathology.

The most relevant clinical and laboratory data at the initial time of emergency admission are shown in table II.

In seven cases the abdominal pain was located on the right abdomen (64%), mainly in the right iliac cavity, and in the remaining three the pain was diffuse in nature. In only one patient the reason for consultation was not abdominal pain but diarrheas and nausea, mimicking an acute gastroenteritis.

Three patients have had self-limited abdominal pain episodes before admission.

In the laboratory work-up, leukocytosis was remarkable, although in some cases we observed normal blood leukocytes counts but with left shift.

In 8 patients (72%) the abdomen X-ray film showed dilated small bowel loops with air-fluid levels.

In 4 patients, abdominal ultrasound was carried out that was unremarkable, only visualizing small bowel loops slightly edematous with decreased peristaltic movements. In two patients, an abdominal CT scan was performed before the surgery yielding images compatible with mesenteric ischemia. In no case fiber colonoscopy was carried out. In five patients occult blood in stools was performed, being positive in three of them.

The time elapsed from the onset on the clinical picture until performance of laparotomy varied from 7 hours to 4 days. The time for making a diagnosis was precisely the longest in the patient presenting with nausea and vomiting.

**Table III. Intestinal areas involved**

Ileum	5 (45%)
Jejunum	1 (9%)
Right colon and caecum	2 (18%)
Sigmoid colon	1 (9%)
Massive*	2 (18%)

\* The term massive comprises the involvement of the whole small bowel and part of the right colon.

The intestinal areas involved are shown in table III, the ileum being the intestinal segment damaged in the highest number of cases.

In the two patients with massive mesenteric ischemia, immediate surgical closure was done because of inviability.

In just one case there was no necrosis of the intestinal wall, with the finding of one segmental lesion of about 15 cm in length at the jejunum, with edema and abundant fibrin within the mesentery. Since it looked viable, local heat was applied with wet compresses for 15 minutes with further closure by planes. The post-surgical period was uneventful, the patient being discharged 21 days after the surgery. In the 8 (73%) cases remaining, there was a more localized intestinal necrosis, performing bowel resection. Of them, six patients died, surviving for a period between 12 hours and 45 days after the surgery. The death causes were: septic shock due to formation on intra-abdominal abscesses (3 cases), surgical suture dehiscence (1), probable recurrence of mesenteric ischemia (1), another one died from nosocomial pneumonia with empyema, and in another one an important retroperitoneal haematoma was evidenced at autopsy.

In the three (27%) patients surviving to mesenteric ischemia, surgical therapy was established in less than 8 hours after the diagnostic suspicion at the emergency room. In those dying, the surgical intervention was delayed between 17 hours and 4 days, except in one patient that was operated 7 hours after admission but that had been having bouts of abdominal pain for three days, and in another one that was operated 10 hours after admission but that had received some years ago right hemicolectomy for neoplasm. The three patients having presented in the past self-limited episodes of abdominal pain died. Two of them presented at laparotomy disseminated peritonitis, in one case from the necrotic wall of the ileum, and in the other case fecaloid peritonitis due to perforation of the sigmoid colon. In the third case, there was necrosis of the whole small bowel and part of the right colon. The clinical presentation was similar in all the cases with the exception of these latter three and the one presenting an onset mimicking an acute gastroenteritis.

## DISCUSSION

Mesenteric ischemia seems to be more common among dialysis patients,<sup>9</sup> being estimated between 0.3%-1.9% per patient/year,<sup>4,10</sup> (0.87% in our series).

The mortality rate is very high and there exist poor prognostic factors.<sup>8</sup> In the present study we highlight the high prevalence of cardiovascular pathology.<sup>11</sup> Table IV shows the death causes in hemodialysis patients at our Hospital for the last 5 years (2002-2006), pointing out that mesenteric ischemia accounts for 6.7% of all deaths during that period.

The epidemiological analysis of the data from the Catalan Register of Kidney Patients has reported a progressive increase in the mortality due to mesenteric ischemia; before the year 1991 it was 0.9% and between 1991-2002, it was 3%.<sup>12</sup>

Besides, several articles have described an increase in its incidence among dialysis patients in recent years,<sup>3,4,10,13,14</sup> likely related to increased survival and, thus, a bigger population

**Table IV.**

Death causes (2002-2006)	Num. of patients and percentage
<i>*Cardiovascular:</i>	
- Sudden death	7 (11.8%)
- Coronary heart disease	5 (8.4%)
- Mesenteric ischemia	4 (6.7%)
- Cerebrovascular accident	2 (3.4%)
	<b>18 (30%)</b>
<i>*Other</i>	41 (70%)
<b>Total</b>	<b>59 (100%)</b>

susceptible of suffering from this disease.<sup>10</sup> At our Center, the patients diagnosed with mesenteric ischemia have been mainly grouped in two year-periods, between 1988-1992 with 5 cases, and between 2002-2006 with 4 cases. It is very likely that a final diagnosis has not been reached sometimes, which is performed by colonoscopy (in the case of ischemic colitis) or laparotomy. Many times urgent colonoscopy is not feasible, and laparotomy has often been delayed due to the high surgical risk in these patients, some of them requiring being transferred to the reference hospital to be surgically treated. In others, the so poor hemodynamic status has precluded performing the laparotomy, and the patients have died with a "high suspicion of mesenteric ischemia".

Throughout the last 19 years, we are aware of three additional cases dying from suspected mesenteric ischemia in whom the surgical intervention was not carried out. All of them had known cardiovascular pathology and high comorbidity. Considering all this, there may be an estimated frequency of mesenteric ischemia among our hemodialysis population of 1.11% per patient/year.

As we have been able to observe, mesenteric ischemia may be difficult to diagnose.<sup>3</sup> The usual clinical picture is abdominal pain, which usually begins 8-12 hours after dialysis, although it may also take place during the hemodialysis session.<sup>10,14,15</sup> In our patients, the abdominal pain started 4-12 hours after the last session except in three that had already had previous episodes of abdominal pain, within a period varying from 3 days to 2 months.

The "subacute" presentation as repeated episodes of abdominal pain is related to poorer prognosis due to longer clinical course and, thus, more disseminated ischemic lesions and/or necrosis of the whole intestinal wall, even with perforation and peritonitis. This is also true for the longer the time elapsed between the clinical onset and the surgical intervention. It is thus essential to suspect this pathology earlier even in the cases with a more subacute pain, and perform an abdominal CT scan and/or fiber colonoscopy that may help with the diagnosis.

None of our patients had fever at the beginning, although in other series of patients the authors point out that fever is as frequent as abdominal pain.<sup>10</sup>

Zeier *et al.* reported that, aside from abdominal pain, most of their patients presented hematochezia, constipation, and tympanites. This latter sign would be particularly present when the intestinal segment involved is the caecum.<sup>3,16</sup>

From the laboratory perspective, leukocytosis is the most frequent finding.<sup>10,11,14</sup> Positive occult blood in the feces may be observed in several cases. Other laboratory parameters frequently used for the diagnosis of mesenteric ischemia in patients not submitted to dialysis, such as hyperphosphatemia, hyperkalemia, metabolic acidosis, and increased LDH and CPK are of little help in our patients because they are difficult to interpret since some of them are already increased due to uremia itself and/or in relation to the time elapsed from the last dialysis session.<sup>17</sup> The possible usefulness of serum lactate levels has also been suggested in mesenteric ischemia.<sup>3</sup>

From a radiological perspective, plain abdominal films are very unspecific, and dilation of small bowel loops and the colon may be observed. In perforated cases, free air may be seen as pneumoperitoneum. For many times, the opaque enema was the first choice diagnostic method, showing "digital printings" corresponding to submucosal edema and hemorrhage.<sup>15</sup> The colonoscopy is a very sensitive test that may locate the lesion and allows gathering tissue samples for the pathology study.<sup>18</sup> It must, however, be carried out very carefully since air insufflations used may cause overpressure and induce new ischemic lesions.<sup>19</sup> Besides, mucosal changes do not indicate the transmural changes, and thus it is a test that helps us making the diagnosis but not assessing the severity of the disease.<sup>15</sup>

As we have pointed out, the abdominal ultrasound does not bring additional information, and abdominal CT scan is not diagnostic by itself, although it may show changes suggestive of mesenteric ischemia, such as wall thickening and distension of the bowel loops. Besides, the revascularization study performed as an additional step may show signs suggestive of thrombosis of the superior or inferior mesenteric arteries according to whether the intestinal segment involved is the small bowel/right colon or the left or descendant colon, respectively. However, in hemodialysis patients, the mesenteric infarction usually is non-occlusive, with permeable vessels. For this reason, the angiogram usually is of little help, few times showing a significant occlusion.<sup>3,10,14,15</sup> The precipitating factors may be the episodes of arterial hypotension occurred during previous dialysis due to the subsequent hypoperfusion and ischemia, which occurred in 6 out of 11 patients in our series. Cases of hypotension and later development of mesenteric ischemia have also been described in dialysis patients having suffered a myocardial infarction or exacerbation of aortic valve stenosis.<sup>16,18</sup> It is important to avoid as much as possible excessive ultrafiltration during the hemodialysis sessions and to assess the possible need for hydration in those dialysis patients having volume depletion because of vomiting, diarrhea, or fever.<sup>6,16</sup> We should also consider that mesenteric ischemia may also happen in peritoneal dialysis patients, particularly in those having excessive drainage volumes many times accompanied by prolonged arterial hypotension states. In these patients, the clinical picture of mesenteric ischemia may mimic peritonitis, and even be misinterpreted with it, delaying even more the diagnosis.<sup>20,21</sup>

Berger *et al.* have shown the usefulness, cost-effectiveness, and lower aggressiveness of the abdominal CT scan with soluble enema to make an early diagnosis, with the capability of assessing the severity of the lesion by differentiating between

ischemia (wall thickening) and necrosis (with intestinal pneumatosis). These radiological characteristics have shown a 100% correlation with surgical findings. Thanks to this test, the authors were able to increase their patients' survival rate.<sup>8,10,15</sup> However, the findings mentioned in both this test and the colonoscopy would be limited to the cases with colonic involvement.

Only one out of 11 patients in our series had left colonic involvement. A higher frequency of involvement of the right colon and the caecum has been reported in dialysis patients.<sup>10,14,15</sup> This intestinal segment seems to be particularly susceptible to non-occlusive ischemia since there is little natural collateral circulation able to keep up with tissular demands in the case of losing the main arterial source.<sup>22</sup> In addition, the right colonic vasa recta are longer and originate from a more distant site than in the left colon, which may increase the resistance to reperfusion after an ischemic insult from arterial hypotension.<sup>23</sup> In our series of patients, the ileum was the intestinal segment more frequently involved, likely due to hypoperfusion at the superior mesenteric artery level, many times due to severe episodes of arterial hypotension.

The administration of several drugs has been related to mesenteric ischemia,<sup>24</sup> as with digital due to its mesenteric vasoconstrictive effect,<sup>25</sup> and ergotamine alkaloids due to the presence of fibrosis around the mesenteric vessels.<sup>26</sup> However, the association with medications inducing constipation as a side effect has particularly been described.<sup>6</sup> Several works have pointed out persistent constipation as a risk factor for mesenteric ischemia;<sup>14,27</sup> this condition may be potentiated with the use of medications such as Resincalcio® (calcium polystyrene sulfonate). In the group of patients described, we have evidence of digoxine prescription in one of them and of Resincalcio® in another one, as well as the occurrence of mesenteric ischemia in two patients after worsening of their usual constipation.

Mesenteric ischemia is usually surgically managed.<sup>4,10,14</sup> Early surgical intervention is associated to better survival.<sup>10,14</sup> In our series, only three patients survived, being operated within less than 8 hours from the onset of the symptoms.

The main death causes during the post-surgical period are extension of the ischemic lesions<sup>4</sup> and septic shock.<sup>14</sup>

To conclude, mesenteric ischemia is uncommon among hemodialysis patients, and most of those presenting it have known cardiovascular pathology that may act as a predisposing factor. This condition should be suspected in every hemodialysis patient with abdominal pain, particularly if the pain is located in the right iliac cavity and there has been a previous episode of arterial hypotension. The presence of leukocytosis, together with positive occult blood in the stools, is a rather unspecific datum, but which may favor making the diagnosis.

Based on our experience, we recommend early surgical intervention within the first 8 hours. Since the small bowel was more frequently and severely involved in our series, and given that there are no conventional radiological tests or diagnostic laboratory parameters, laparoscopy or laparotomy should be mandatory if mesenteric ischemia is suspected and there is no absolute contraindication for carrying them out. For these reasons, the intervention of nephrologists and sur-

geons familiar with abdominal pathology in uremic patients is paramount since only early diagnosis may prevent these patients from dying of this life-threatening emergency.

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