

Higher risk of renal disease in chronic hepatitis C patients and antiviral therapy survival benefit in patients on hemodialysis

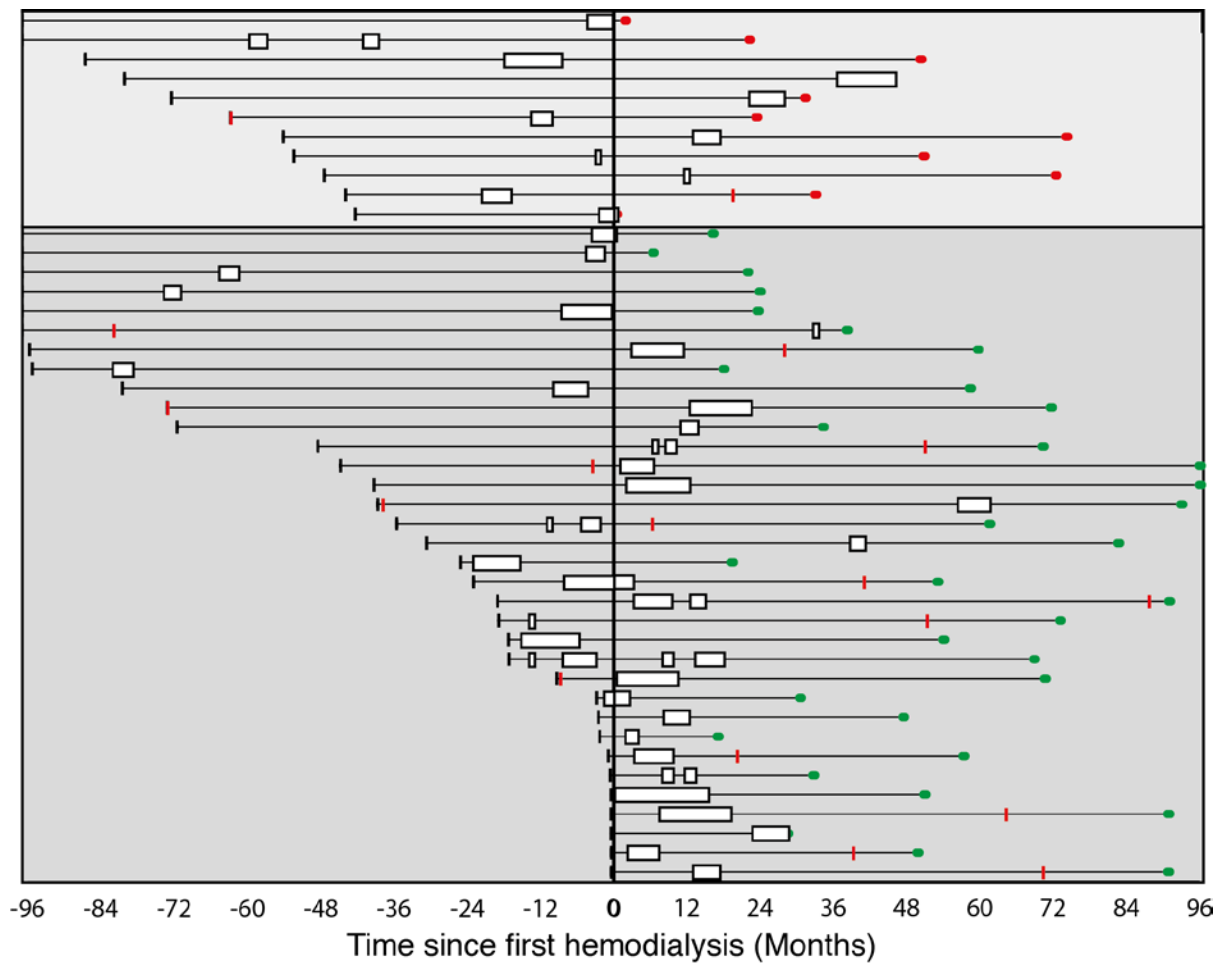
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Fig. S1



Each line represents 1 patient, with time zero indicating HD initiation. The line starts at CHC diagnosis and ends either at death (red circle) or study end (green circle). The white boxes represent patients on HCV treatment, with the size depending on the duration the patients would be on HCV treatment if they took all dispensed drugs according to the product insert. The red bars indicate if and the time for kidney transplantation. The patients were grouped depending whether they were alive or dead.

Supplemental Tables

Table S1. Cause of Death per ICD-10 Chapter and the 10 Most Common Causes of Death in All Patients With CHC and CKD and After the 6-Month Lag Period

Chapter	Definition	CKD/CHC (n=559)	After 6-month lag period (n=310)
I (A00-B99)	Certain infectious and parasitic diseases	68 (12%)	40 (13%)
II (C00-D48)	Neoplasms	57 (10%)	34 (11%)
III (D50-D89)	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	3 (0.5%)	2 (0.7%)
IV (E00-E90)	Endocrine, nutritional and metabolic diseases	65 (12%)	28 (9%)
V (F00-F99)	Mental and behavioral disorders	11 (2%)	9 (3%)
VI (G00-G99)	Diseases of the nervous system	1 (0.2%)	-
IX (I00-I99)	Diseases of the circulatory system	162 (29%)	87 (28%)
X (J00-J99)	Diseases of the respiratory system	10 (2%)	6 (2%)
XI (K00-K93)	Diseases of the digestive	54 (10%)	46 (15%)

	system		
XII (L00-L99)	Diseases of the skin and subcutaneous tissue	1 (0.2%)	1 (0.3%)
XIII (M00-M99)	Diseases of the musculoskeletal system and connective tissue	4 (0.7%)	3 (1%)
XIV (N00-N99)	Diseases of the genitourinary system	70 (13%)	25 (8%)
XVII (Q00-Q99)	Congenital malformations, deformations and chromosomal abnormalities	13 (2%)	8 (3%)
XVIII (R00-R99)	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	13 (2%)	6 (2%)
XX (V01-Y98)	External causes of morbidity and mortality	27 (5%)	15 (5%)

Ccauses of death - top 10 all CKD/CHC patients

ICD code	Definition	CKD/CHC (n=559)	After 6-month lag period (n=310)
B18.2	Chronic hepatitis C	43 (8%)	27 (9%)
I21.9	Acute myocardial infarction, unspecified	34 (6%)	18 (6%)
N18.9	Chronic kidney disease,	27 (5%)	10 (3%)

	unspecific		
N19	Unspecific kidney failure	20 (4%)	9 (3%)
	Unspecific diabetes mellitus	18 (3%)	8 (3%)
E14.2	with renal complications		
	Chronic ischemic heart	16 (3%)	10 (3%)
I25.9	disease, unspecified		
	Unspecified diabetes mellitus	13 (2%)	5 (2%)
E14.9	without complications		
	Other forms of chronic	13 (2%)	8 (3%)
I25.8	ischemic heart disease		
I25.1	Atherosclerotic heart disease	12 (2%)	7 (2%)
	Other and unspecified cirrhosis	11 (2%)	8 (3%)
K74.6	of liver		

Causes of death - top 10 after lag period

ICD code	Definition	CKD/CHC (n=559)	After 6-month lag period (n=310)
B18.2	Chronic Hepatitis C	43 (8%)	27 (9%)
I21.9	Acute myocardial infarction, unspecific	34 (6%)	18 (6%)
I25.9	Chronic ischemic heart disease, unspecified	16 (3%)	10 (3%)
N18.9	Chronic Kidney Disease, unspecific	27 (5%)	10 (3%)
N19	Unspecific kidney failure	20 (4%)	9 (3%)

I25.8	Other forms of chronic ischemic heart disease	13 (2%)	8 (3%)
K74.6	Other and unspecified cirrhosis of liver	11 (2%)	8 (3%)
E14.2	Unspecific diabetes mellitus with renal complications	18 (3%)	8 (3%)
C22.0	Hepatocellular carcinoma	9 (2%)	7 (2%)
I25.1	Atherosclerotic heart disease	12 (2%)	7 (2%)

CHC=chronic hepatitis C; CKD=chronic kidney disease; ICD=International Classification of Diseases.

Table S2. Cause of Death per ICD-10 Chapter and the 11 Most Common Causes of Death for patients in the Compator Cohort With a CKD diagnosis

(n=463/1,454; 32%)

Chapter	Definition	CKD (n=463)
I (A00-B99)	Certain infectious and parasitic diseases	14 (3%)
II (C00-D48)	Neoplasms	72 (16%)
III (D50-D89)	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	2 (0.5%)
IV (E00-E90)	Endocrine, nutritional and metabolic diseases	51 (11%)
V (F00-F99)	Mental and behavioral disorders	8 (2%)
VI (G00-G99)	Diseases of the nervous system	5 (1%)
IX (I00-I99)	Diseases of the circulatory system	201 (43%)
X (J00-J99)	Diseases of the respiratory system	19 (4%)
XI (K00-K93)	Diseases of the digestive system	24 (5%)

XIII (M00-M99)	Diseases of the musculoskeletal system and connective tissue	5 (1%)
XIV (N00-N99)	Diseases of the genitourinary system	31 (7%)
XVII (Q00-Q99)	Congenital malformations, deformations and chromosomal abnormalities	4 (0.9%)
XVIII (R00-R99)	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	17 (4%)
XX (V01-Y98)	External causes of morbidity and mortality	10 (2%)

ICD code	Definition	CKD (n=463)
I21.9	Acute myocardial infarction, unspecified	50 (11%)
I25.9	Chronic ischemic heart disease, unspecified	17 (4%)
E14.9	Unspecified diabetes mellitus without complications	14 (3%)
N18.9	Chronic kidney disease, unspecified	14 (3%)
I25.1	Atherosclerotic heart disease	11 (2%)

	Other forms of chronic	10 (2%)
I25.8	ischemic heart disease	
	Ill-defined and unknown cause	10 (2%)
R99.9	of mortality	
	Malignant neoplasm of	9 (2%)
	unspecified part of bronchus or	
C34.9	lung	
E14.2	Unspecific diabetes mellitus	9 (2%)
	with renal complications	
	Unspecific diabetes mellitus	9 (2%)
E14.7	with multiple complications	
I42.0	Dilated cardiomyopathy	9 (2%)

CHC=chronic hepatitis C; CKD=chronic kidney disease; ICD=International Classification of Diseases.

Table S3. CHC in HD Patients in Sweden per Year between 2010 and 2013

	2010	2011	2012	2013
In-hospital HD patients[1]	2,824	2,929	2,911	2,881
Patients with CHC on in-hospital HD	112	110	99	87
Percentage of in-hospital HD patients with CHC	4.0%	3.8%	3.4%	3.0%

CHC=chronic hepatitis C; HD=hemodialysis.

Table S4. Cause of Death per ICD-10 Chapter and Causes for HCV Treated and Not Treated Patients on HD

Chapter	Definition	No HCV treatment (n=124)	HCV treated (n=11)
I (A00-B99)	Certain infectious and parasitic diseases	7 (6%)	-
II (C00-D48)	Neoplasms	8 (6%)	1 (9%)
IV (E00-E90)	Endocrine, nutritional and metabolic diseases	18 (15%)	3 (27%)
V (F00-F99)	Mental and behavioral disorders	2 (2%)	-
IX (I00-I99)	Diseases of the circulatory system	33 (27%)	4 (36%)
X (J00-J99)	Diseases of the respiratory system	4 (3%)	-
XI (K00-K93)	Diseases of the digestive system	13 (10%)	2 (18%)
XIV (N00-N99)	Diseases of the genitourinary system	24 (19%)	1 (19%)
XVII (Q00-Q99)	Congenital malformations, deformations and chromosomal abnormalities	5 (4%)	-
XVIII (R00-	Symptoms, signs and	3 (6%)	-

R99)	abnormal clinical and laboratory findings, not elsewhere classified		
XX (V01-Y98)	External causes of morbidity and mortality	7 (6%)	-
<u>Causes of death</u>			
ICD code	Definition	No HCV treatment (n=124)	HCV treated (n=11)
A41.9	Sepsis, unspecified organism	1 (0.8%)	-
B18.2	Chronic hepatitis C	6 (5%)	-
C16.0	Malignant neoplasm of cardia	1 (0.8%)	-
C22.9	Malignant neoplasm of liver, not specified as primary or secondary	2 (2%)	-
C34.9	Malignant neoplasm: bronchus or lung, unspecified	-	1 (9%)
C64	Malignant neoplasm of kidney, except renal pelvis	1 (0.8%)	-
C67.9	Malignant neoplasm of bladder, unspecified	1 (0.8%)	-
C80.0	Disseminated malignant neoplasm, unspecified	1 (0.8%)	-
C90.0	Multiple myeloma	1 (0.8%)	-
E10.0	Type 1 diabetes mellitus with	-	1 (9%)

	coma		
E10.2*	Type 1 diabetes mellitus with renal complications	1 (0.8%)	-
E11.2*	Type 2 diabetes mellitus with renal complications	3 (2%)	1 (9%)
E11.6	Type 2 diabetes mellitus with other specified complications	1 (0.8%)	-
E14.2*	Unspecific diabetes mellitus with renal complications	6 (5%)	-
E14.5	Unspecified diabetes mellitus with circulatory complications	1 (0.8%)	-
E14.7	Unspecified diabetes mellitus with multiple complications	1 (0.8%)	-
E14.8	Unspecified diabetes mellitus with unspecified complications	2 (2%)	-
E14.9	Unspecified diabetes mellitus without complications	3 (2%)	1 (9%)
F19.1	Other psychoactive substance abuse	2 (2%)	-
I08.0	Rheumatic disorders of both mitral and aortic valves	1 (0.8%)	-
I12.0*	Hypertensive renal disease with renal failure	4 (3%)	-
I13.1*	Hypertensive heart and renal disease with renal failure	1 (0.8%)	-

I13.2*	Hypertensive heart and renal disease with both (congestive) heart failure and renal failure	1 (0.8%)	-
I21.9	Acute myocardial infarction, unspecified	7 (6%)	-
I25.1	Atherosclerotic heart disease	1 (0.8%)	1 (9%)
I25.8	Other forms of chronic ischemic heart disease	2 (2%)	-
I25.9	Chronic ischemic heart disease, unspecified	5 (4%)	1 (9%)
I33.0	Acute and subacute infective endocarditis	1 (0.8%)	-
I35.0	Nonrheumatic aortic (valve) stenosis	2 (2%)	-
I38	Endocarditis, valve unspecified	-	1 (9%)
I42.6	Alcoholic cardiomyopathy	1 (0.8%)	-
I61.9	Intracerebral hemorrhage, unspecified	1 (0.8%)	1 (9%)
I63.5	Cerebral infarction due to unspecified occlusion or stenosis of cerebral arteries	1 (0.8%)	-
I64	Stroke, not specified as haemorrhage or infarction	1 (0.8%)	-
I70.1	Atherosclerosis of renal artery	1 (0.8%)	-
I70.9	Other and unspecified	1 (0.8%)	-

	atherosclerosis		
I71.9	Aortic aneurysm of unspecified site, without rupture	1 (0.8%)	-
I72.8	Aneurysm of other specified arteries	1 (0.8%)	-
J18.1	Lobar pneumonia, unspecified organism	1 (0.8%)	-
J18.9	Pneumonia, unspecified organism	1 (0.8%)	-
J44.0	Chronic obstructive pulmonary disease with acute lower respiratory infection	1 (0.8%)	-
J84.1	Other interstitial pulmonary diseases with fibrosis	1 (0.8%)	-
K25.4	Gastric ulcer, chronic or unspecified with hemorrhage	-	1 (9%)
K55.0	Acute vascular disorders of intestine	1 (0.8%)	-
K56.5	Intestinal adhesions [bands] with obstruction	1 (0.8%)	-
K56.7	Ileus, unspecified	1 (0.8%)	-
K65.9	Peritonitis, unspecified	1 (0.8%)	-
K70.3	Alcoholic cirrhosis of liver with ascites	1 (0.8%)	-
K72.9	Hepatic failure, unspecified	1 (0.8%)	-

K74.6	Other and unspecified cirrhosis of liver	2 (2%)	1 (9%)
K75.0	Abscess of liver	1 (0.8%)	-
K80.1	Calculus of gallbladder with other cholecystitis	1 (0.8%)	-
K81.0	Acute cholecystitis	1 (0.8%)	-
K83.9	Disease of biliary tract, unspecified	1 (0.8%)	-
K92.2	Gastrointestinal hemorrhage, unspecified	1 (0.8%)	-
N02.8*	Recurrent and persistent hematuria with other morphologic changes	1 (0.8%)	-
N03.9*	Chronic nephritic syndrome with unspecified morphologic changes	2 (2%)	-
N05.5*	Unspecified nephritic syndrome: diffuse mesangiocapillary glomerulonephritis	1 (0.8%)	1 (9%)
N05.9*	Unspecified nephritic syndrome with unspecified morphologic changes	1 (0.8%)	-
N11.9	Chronic tubulo-interstitial nephritis, unspecified	1 (0.8%)	-

N18.9*	Chronic kidney disease, unspecific	8 (6%)	-
N19*	Unspecific kidney failure	8 (6%)	-
N28.8	Other specified disorders of kidney and ureter	1 (0.8%)	-
N39.0	Urinary tract infection, site not specified	1 (0.8%)	-
Q61.3	Polycystic kidney, unspecified	4 (3%)	-
Q87.8	Other specified congenital malformation syndromes, not elsewhere classified	1 (0.8%)	-
R99	Ill-defined and unknown cause of mortality	3 (2%)	-
W19	Unspecified fall	1 (0.8%)	-
X09	Exposure to unspecified smoke, fire and flames	1 (0.8%)	-
X40	Accidental poisoning by and exposure to nonopioid analgesics, antipyretics and antirheumatics	1 (0.8%)	-
X42	Accidental poisoning by and exposure to narcotics and psychodysleptics [hallucinogens], not elsewhere classified	1 (0.8%)	-

X59.0	Exposure to unspecified factor causing fracture	1 (0.8%)	-
Y12	Poisoning by and exposure to narcotics and psychodysleptics [hallucinogens], not elsewhere classified, undetermined intent	1 (0.8%)	-
Y83.5	Amputation of limb(s)	1 (0.8%)	-

*=Included in the competing risk analysis; HCV=hepatitis C virus; HD=hemodialysis;

ICD=International Classification of Diseases.

Table S5. Cause of Death per ICD-10 Chapter and Top 11 Causes for patients in the Compator Cohort on HD (n=79/205; 39%)

Chapter	Definition	HD (n=79)
I (A00-B99)	Certain infectious and parasitic diseases	3 (4%)
II (C00-D48)	Neoplasms	10 (13%)
IV (E00-E90)	Endocrine, nutritional and metabolic diseases	11 (14%)
V (F00-F99)	Mental and behavioral disorders	1 (1%)
IX (I00-I99)	Diseases of the circulatory system	36 (46%)
X (J00-J99)	Diseases of the respiratory system	1 (1%)
XI (K00-K93)	Diseases of the digestive system	4 (5%)
XIII (M00-M99)	Diseases of the musculoskeletal system and connective tissue	2 (3%)
XIV (N00-N99)	Diseases of the genitourinary system	6 (8%)
XVII (Q00-Q99)	Congenital malformations, deformations and chromosomal abnormalities	2 (3%)

XVIII (R00- R99)	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	3 (4%)
ICD code	Definition	HD (n=79)
I21.9	Acute myocardial infarction, unspecific	10 (13%)
I12.0	Hypertensive renal disease with renal failure	4 (5%)
E14.2	Unspecific diabetes mellitus with renal complications	3 (4%)
	Unspecific diabetes mellitus	3 (4%)
E14.7	with multiple complications	
I42.0	Dilated cardiomyopathy	3 (4%)
I61.9	Nontraumatic intracerebral hemorrhage, unspecified	3 (4%)
N18.9	Chronic kidney disease, unspecific	3 (4%)
	Malignant neoplasm of unspecified part of bronchus or lung	2 (3%)
C34.9		
C90.0	Multiple myeloma	2 (3%)
Q61.3	Polycystic kidney, unspecified	2 (3%)
R99.9	Ill-defined and unknown cause of mortality	2 (3%)

HCV=hepatitis C virus; HD=hemodialysis; ICD=International Classification of Diseases.

References

[1] SNR. SNR Årsrapport 2014_Webb.pdf. 2014.